Vol. 20 No. 102 June, 1945

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ARCHIVES OF DISEASE IN CHILDHOOD

INCORPORATING THE BRITISH JOURNAL OF CHILDREN'S DISEASES

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LONDON
BRITISH MEDICAL ASSOCIATION
TAVISTOCK SQUARE, W.C.1

Yearly Subscription (4 Numbers) 25/- U.S.A. $6.00 Single Number 7/6

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THOMAS BARLOW, 1845–1945

ADDRESS BY SIR ROBERT HUTCHISON

On the occasion of the Memorial Service

Held at the Hospital for Sick Children, Great Ormond Street, on Wednesday, March 7, 1945

We are met here to-day in thankful remembrance of the life and work of Thomas Barlow. A memorial service has already been held for him elsewhere which was largely attended by his many friends both lay and medical, but it is fitting that we should have our own simple service here in the Hospital to which he was so much devoted and where much of his best work was done.

We may look upon it, I think, as a form of family worship and recollection for at this Hospital, above most, all who are associated with it feel themselves to be one of a family. It is difficult to realize that it is 70 years since he whom we have in our thoughts to-day first joined this family when he became Assistant Physician to the Hospital and that he served it faithfully thereafter for a period of nearly 25 years and perhaps my only claim to address you this afternoon is that I had the privilege of acting as his House Physician here almost half a century ago. So much, however, did his life exceed the ordinary human span that a generation and a half have elapsed since his retirement from our staff and to many here present, I dare say, he was known only as the Father of our profession and as a venerated and, latterly at least, almost legendary figure; but we remember with pride that he was essentially a Great Ormond Street man and that to the end of his life the Hospital for Sick Children held a high place in his affections.

The generations rise and pass away and most of us are soon forgotten for, as another great medical Sir Thomas said, 'the iniquity of oblivion blindly scattereth her poppy', but those few of whom the memory survives are remembered either for their work or for their character; for what they did or for what they were.

We may feel sure that the name of Thomas Barlow will live on both grounds; he earned a permanent place in medical history by his original work, especially in diseases of children, and through the term 'Barlow's disease', which is used on the Continent, he obtained an eponymous immortality. At the same time in the daily practice of his profession he was completely successful and will long be remembered as perhaps the most popular Consulting Physician of the late Victorian epoch. As Dr. Johnson said of Mead—on the site of whose house we are assembled to-day—'no one ever lived more in the full sunshine of life' and his professional opinion was sought by the highest in the land. But though he 'walked with kings' he never 'lost the common touch' and I well remember his saying to me once when he was at the very height of his fame that he sometimes felt he would like to give it all up and work only amongst poor folk. His skill was only matched by his kindness and sympathy for he was not one who ever lost sight of the 'patient' in the 'case'! He was always ready, too, to extend a helping hand to his less fortunate professional brethren who had fallen by the way, or on whom misfortune had come, and his work for the Royal Medical Benevolent Fund on their behalf is known to all. He was in very truth the Beloved Physician, who did justly, loved mercy and walked humbly, quite unspoilt by success.

No one ever obeyed more faithfully that sentence in the Hippocratic Oath binding on all who practise medicine, which enjoins us to 'Keep holy both the life and the art'. Nor had he any need—for in his case it had already been answered—to offer up the prayer of that great Jewish physician of the 12th century, Maimonides:

'. . . Let me be intent on one thing, O Father of Mercy, to be always merciful to thy suffering children. . . . That I may be able to devote myself, body and soul, to thy children who suffer pain.'

May all who serve this Hospital be given grace and strength to follow in his footsteps.

A HANDLIST OF THE WRITINGS OF SIR THOMAS BARLOW

Compiled by ALFRED WHITE FRANKLIN, M.B., F.R.C.P.

Barlow wrote chiefly of disease as he saw it in the organs and tissues of his patients, living and dead. Nothing but his classic papers on scurvy will escape the dusty, unread fate of medical ephemera. This handlist preserves at least the names of those medical things that caught his eye and mind; another list, as long, could record meetings attended and speeches made to help his fellow men.

1. On a case of pericardial effusion, in which paracentesis was performed *Practitioner*, 1873, **11,** 265–270.
2. Aneurysm at base of left ventricle of heart *Trans. Path. Soc. Lond.*, 1875, **26,** 65–6.
3. Case of acute tuberculosis in a child aged four months *Brit. med. J.*, 1876, **2,** 552.
4. Congenital heart disease; two cases *Trans. path. Soc. Lond.*, 1876, **27,** 140–2.
5. On a case of tubercle of the pancreas *Loc. cit.*, 173–5.
6. Receding gummata of liver in case of congenital syphilis *Loc. cit.*, 202–3.
7. Case of phlegmonous syphilides *Lancet*, 1876, **2,** 637.
8. Case of sporadic haemophilia *Med. Times Gaz.*, 1876, **2,** 591–2.
9. Membranous ophthalmia, confined to one eye *Loc. cit.*, 623.
10. On a case of double hemiplegia, with cerebral symmetrical lesions *Brit. med. J.*, 1877, **2,** 103–4.
11. Brain of a microcephalous child *Trans. path. Soc. Lond.*, 1877, **28,** 8–9.
12. Meningitis, arteritis, and choroiditis in a child the subject of congenital syphilis *Loc. cit.*, 287–291.
13. Gummata on cranial nerves; disease of cerebral arteries; cicatrices of liver and spleen in a case of congenital syphilis *Loc. cit.*, 291–5 1 plate.
14. Enlargement of the spleen and heart disease in a case of congenital syphilis *Loc. cit.*, 353–6.
15. Note on cerebral aneurism subsequent to emboli *Med. Times Gaz.*, 1877, **1,** 362.
16. Double otitis—meningitis *Loc. cit.*, 390–1.
17. Case of hysteria with hemianaesthesia and ovarian hyperaesthesia of the opposite side *Loc. cit.*, 537.
18. Alopecia in congenital syphilis *Lancet*, 1877, **2,** 276–7.
19. Notes on pleuritic effusion in childhood (T. B. and R. W. Parker) *Brit. med. J.*, 1877, **2,** 758–760.
20. Case of undescribed eruption in a tuberculous child *Trans. clin. Soc. Lond.*, 1877, **10,** 196–8.
21. A case of ovariotomy in a child aged twelve years (T. B. and H. Marsh) *Ibid.*, 1878, **11,** 175–9.
22. Analgesia as a diagnostic test of hysteria *Med. Times Gaz.*, 1878, **1,** 191–2.
23. On the cervical opisthotonos of infants (S. Gee and T. B.) *St. Bart's Hosp. Rep.*, 1878, **14,** 23–42 See *Proc. roy. med.-chir. Soc.*, 1896–7, **1,** 114–7.
24. Note on frequency of pleural effusion in infancy *Lancet*, 1878, **2,** 877.
25. Case of urticaria pigmentosa *Trans. clin. Soc. Lond.*, 1879, **12,** 72–4.
26. Specimens of bronchial gland disease *Trans. path. Soc. Lond.*, 1879, **30,** 254–7.
27. Enlargement of bronchial glands with relation to whooping cough *Brit. med. J.*, 1879, **2,** 889.
28. Congenital heart disease; pulmonary stenosis, with dilated pulmonary artery above the stenosis *Trans. path. Soc. Lond.*, 1879, **30,** 272–3.
29. Specimens of craniotabes *Loc. cit.*, 332–3.
30. Specimens of disease of skull in congenital syphilis *Loc. cit.*, 333–9. 1 plate.
31. On lesions of the cranial bones in congenital syphilis (illustrated by three living cases) (T. B. and D. B. Lees) *Loc. cit.*, 350–3.
32. Atelectasis of lungs with emphysematous cyst; congenital heart disease *Trans. path. Soc. Lond.*, 1880, **31,** 48–9.
33. Acute dilatation of heart after scarlatinal dropsy—(?) cardiac thrombosis—right hemiplegia *Med. Times Gaz.*, 1880, **1,** 426–7.
34. *Letter on* The Manchester Children's Hospital and Dr. Humphreys *Brit. med. J.*, 1880, **1,** 186.
35. Laryngitis in congenital syphilis *Trans. path. Soc. Lond.*, 1880, **31,** 46–8.
36. Malformation of the heart . . . (T. B. Peacock and T. B.) *Loc. cit.*, 91.
37. Gumma of tongue in hereditary syphilis *Loc. cit.*, 101–2.
38. Disease of growing ends of shafts of long bones in congenital syphilis *Loc. cit.*, 229–233.
39. Cranio-tabes associated with congenital syphilitic disease of parietal bone *Loc. cit.*, 236–8.
40. Case of Addison's disease . . . *Med. Times Gaz.*, 188!, **1,** 124.
41. Pneumonia in an alcoholic subject *Loc. cit.*, 187.
42. Scarlatinal nephritis—meningitis—recovery *Loc. cit.*, 647–8.
43. Hysterical analgesia in children *Brit. med. J.*, 1881, **2,** 892–3.
44. Relationship of craniotabes to rickets and congenital syphilis (D. B. Lees and T. B.) *Trans. path. Soc. Lond.*, 1881, **32,** 323–8 : also *Med. Times Gaz.*, 1880, **2,** 611–6.
45. A case of so-called foetal rickets (cretinism) [dyschondroplasia] *Loc. cit.*, 364–8 1 plate.
46. On subcutaneous nodules connected with fibrous structures, occurring in children the subjects of rheumatism and chorea (T. B. and F. Warner) *Trans. Int. Congr. med. Lond.*, 1881, **4,** 116–128 Reported *Brit. med. J.*, 1881, **2,** 554.
47. Collective investigation committee, Memorandum on acute rheumatism (J. F. Goodhart and T. B.) *Brit. med. J.*, 1882, **1,** 594–5.
48. Memorandum on inherited and acquired syphilis (C. Macnamara and T. B.) *Ibid.*, 1882, **2,** 1228–1230.
49. Case of extirpation of the kidney for calculous pyelitis (T. B. and R. J. Godlee) *Trans. clin. Soc. Lond.*, 1882, **15,** 134–140.
50. [Case of cleido-cranial dysostosis] *Proc. roy. med.-chir. Soc.*, 1882, n.s. **1,** 135.
51. Notes on rheumatism and its allies in childhood *Brit. med. J.*, 1883, **2,** 509–514.
52. On cases described as " acute rickets " which are probably a combination of scurvy and rickets, the scurvy being an essential, and the rickets a variable, element *Med.-chir. Trans.*, 1883, **66,** 159–220 1 plate Abstracted *Proc. roy. med.-chir. Soc.*, 1882–3, n.s. **1,** 102–4 Reported *Brit. med. J.*, 1883, **1,** 619: *Med. Times Gaz.*, 1883, 1, 395: *St. Louis Cour. Med.*, 1883, **9,** 453–5 Reprinted *Arch. Dis. Childh.*, 1935, **10,** 223–252.
53. *Discussion on* Tubercle of the eye *Trans. ophthal. Soc. U.K.*, 1883, **3,** 132–5 See *Lancet*, 1883, **2,** 924.
54. Three cases of Raynaud's disease *Trans. clin. Soc. Lond.*, 1883, **16,** 179–188.
55. Sclerema neonatorum *Loc. cit.*, 262–3.
56. Case of maniacal delirium treated by the cold douche *Lancet*, 1884, **1,** 9–10.
57. Case of purpura occurring in the course of typhoid fever *Loc. cit.*, 745–7.
58. Case of congenital xanthelasma palpebrarum *Trans. path. Soc. Lond.*, 1884, **35,** 405–7 1 plate.
59. Limb-bones, skull, and brain of a case of so-called foetal rickets (? foetal cretinism) *Loc. cit.*, **35,** 459–464.

60. Simple atrophy of the suprarenal capsules and gumma of kidney in a case of Addison's disease *Trans. path. Soc. Lond.*, 1885, **36,** 433–6
61. Sequel to paper on three cases of Raynaud's disease *Trans. clin. Soc. Lond.*, 1885, **18,** 307–312.
62. A case of suppuration around the vermiform appendix treated by abdominal incision (T. B. and R. J. Godlee) *Trans. clin. Soc. Lond.*, 1886, **19,** 88–94: *Brit. med. J.*, 1885, **2,** 1063: *Lancet*, 1885, **2,** 1143: *Med. Times Gaz.*, 1885, **2,** 852.
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64. Ulcers of stomach in a child the subject of general tuberculosis *Trans. path. Soc. Lond.*, 1887, **38,** 141–2.
65. *Translation of* On local asphyxia and symmetrical gangrene of the extremities by Maurice Raynaud IN SELECTED MONOGRAPHS London: The New Sydenham Society, 1888 [iv], 183 Appendix by the translator 184–199.
66. On a case of acute enlargement of the thyroid in a child *Trans. clin. Soc. Lond.*, 1888, **21,** 67–72
67. Case of erythema iris *Illustrated med. News, Lond.*, 1888, **1,** 1–2 1 plate.
68. Case of an infant showing signs of rickets, which had probably started during intra-uterine life, continued after birth for a time, and then undergone partial retrogression *Trans. clin. Soc.* Lond., 1888, **21,** 290–3.
69. Case of diabetes mellitus, in which skin lesions consisting of broad papules and tubercles (? lichen diabeticus) occurred . . . *Brit. J. Derm.*, 1888–9, **1,** 3–9 In German *Mh. prakt. Derm.*, 1888, **7,** 1172–1180.
70. Case of cured subclavian aneurysm *Trans. clin. Soc. Lond.*, 1888–9, **22,** 310–3.
71. Case of hemiatrophy of tongue with paralysis of soft palate following an injury to the upper cervical spine, and (?) to the rim of the foramen magnum *Loc. cit.*, 322–7 1 plate.
72. Case of chronic arthritis in a child, characterized by fibrous contraction of several joints and associated with some thickening of the middle of each tibia and with marked enlargement of groups of lymphatic glands *Loc. cit.*, 328–333.
73. Three cases of Raynaud's disease *Loc. cit.*, 413–4.
74. Pseudo-hypertrophic paralysis, with remarkable secondary atrophy and contraction of the muscles of one lower limb *Illustrated med. News, Lond.*, 1889, **2,** 97–8.
75. Some cases of Raynaud's disease *Ibid.*, **3,** 73–5, 97–100, 125, 176-8 2 plates.
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77. University College Hospital : Introductory Address *Lancet*, 1890, **2,** 735–6
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80. On the prognosis of chronic alcoholism in the light of its pathology *Med. Chron.*, 1892–3, **17,** 215–225.
81. Some clinical remarks on cases in the children's ward of University College Hospital *Clin. J.*, 1893, **1,** 125–8 Reprinted *Ibid.*, 1895, **6,** 373–6.
82. The Bradshaw lecture on infantile scurvy and its relation to rickets *Brit. med. J.*, 1894, **2,** 1029–1034: *Lancet*, 1894, **2,** 1075–1080 In German *Zbl. inn. Med.*, 1895, **16,** 505, 529.
83. Primary atrophy of muscles of limbs and trunk Reported *Brit. med. J.*, 1894, **2,** 1109: *Lancet*, 1894, **2,** 1157.
84. *Discussion on* Congenital syphilitic manifestations in bones and joints *Brit. med. J.*, 1895, **2,** 699 The nervous sequelae of infectious disease *Loc. cit.*, 706.
85. Non-tuberculous posterior basic meningitis in infants *Ibid.*, 1897, **1,** 1091.
86. Case of myopathy, with autopsy, in a boy aet. 5. Sequel to a case shown as living specimen before the Clinical Society, November, 1894 (T. B. and F. E. Batten) *Trans. clin. Soc. Lond.*, 1899, **32,** 98–106 5 plates.
87. Articles on Raynaud's disease (**6,** 577–607 1 plate): Erythromelalgia (**6,** 607–621) : Tuberculous meningitis (**7,** 466–491): Simple meningitis in children (D. B. Lees and T. B.) (**7,** 492–559 1 plate): In A SYSTEM OF MEDICINE, edited by T. C. Allbutt, London, 1899.
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89. Les progrès de la médecine *Rev. sci., Paris*, 1902, 4*s.*, **18,** 225–235.
90. Inheritance of recurrent attacks of jaundice and of abdominal crises, with hepato-splenomegaly (T. B. and H. Batty-Shaw) *Trans. clin. Soc. Lond.*, 1902, **35,** 155–163.
91. The study of the natural history of disease, the basis of all advance in its treatment *Brit. med. J.*, 1902, **2,** 313-321: *Lancet*, 1902, **2,** 267–274.
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93. An address on the hospital ideal and on the concentration of early medical studies in London *Brit. med. J.*, 1904, **2,** 1–4.
94. The present position of the medical profession in relation to alcohol *Quart. J. Inebr.*, 1905, **27,** 234–240.
95. On some of the nervous complications of the specific fevers *Brain*, 1906, **29,** 303–331.
96. *Appreciation of* Sir William Broadbent *Brit. med. J.*, 1907, **2,** 179–180.
97. Presidential address (the work of the Clinical Society of London) *Proc. roy. Soc. Med.* (*clin. sec.*), 1907–8, **1,** 1–8.
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99. *Introduction to* A SCHOOL FOR MOTHERS, published by Horace Marshall Reviewed *Brit. med. J.*, 1907, **2,** 1787.
100. *Note on* Thomas Laurence Read, M.R.C.S. *Brit. med. J.*, 1909, **1,** 379.
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103. *Discussion on* Polioencephalitis and poliomyelitis *Brit. med. J.*, 1913, **2,** 483.
104. *Letter on* Forcible feeding of suffragettes *The Times* Nov. 15, 1913 Reported *Loc. cit.*, 1393.
105. The annual address delivered to the Royal College of Physicians on April 6, 1914 London 1914 8° 28 pp.
106. *Appreciation of* Arthur E. Barker *Brit. med. J.*, 1916, **1,** 638.
107. Harvey, the man and physician *Ibid.*, 1916, **2,** 577–583: *Lancet*, 1916, **2,** 739–746.
108. *Appreciation of* Sir Victor Horsley *Brit. med. J.*, 1916, **2,** 166.
109. Address to the Incorporated Association of Headmasters on the incidence of venereal disease and its relation to school life and school teaching Reported *Ibid.*, 1917, **2,** 797.
110. *Obituary of* W. A. Sturge (1850–1919) *Brit. med. J.*, 1919, **1,** 468: *Lancet*, 1919, **1,** 633: *Med. Pr.*, 1919, n.s. **107,** 284.
111. Introduction *Arch. Dis. Childh.*, 1926, **1,** i–vi.
112. Speech supporting the Presidential speech of thanks, Third International Pediatric Congress, London, 1933 *Acta Paediatr., Stockh.*, 1933, **16,** xxxii.

THE ASSESSMENT OF HEALTH IN CHILDHOOD *

BY

NORMAN B. CAPON, M.D., F.R.C.P.

Professor of Child Health, and Director of the Department of Child Health, University of Liverpool.

The assessment of health in childhood is a task which doctors are called upon to perform in various circumstances, and these may be considered in three main categories:—

1. **The assessment of 'individual' health.** One child is under consideration; the judge is usually the family practitioner or a consultant (general physician, paediatrician or specialist). It may be that the child is ill and the doctor has to decide whether health is improving or deteriorating. It may be that the child's parents believe him to be well and they ask whether their view is correct.

2. **The assessment of 'group' health (A).** A relatively small group of children is under consideration, e.g. the pupils of a certain school; the judge is the medical officer in charge of the health of the group, e.g. a school medical officer. He cannot be expected to study each child as closely as is done in 1 (above), and there are some who consider that it would be undesirable for him to do so because the public (including children) still associates doctors with the idea of disease, and particular care should be taken to avoid causing neurosis in children. Yet his examination of the child must be modelled upon the technique and methods used in 1 (above); and his duty is not confined to the assessment of each individual child's soundness, for he must also concern himself with the state of health of the children as a group and with the practical measures necessary to maintain good health.

3. **The assessment of 'group' health (B).** Under this heading come questions of health in respect of large numbers of children, e.g. all those who live in a certain city or county; the health of all children of a certain age-period in a country, such as neonatal health. The judge is often a medical statistician, or an epidemiologist, or a medical administrative officer; and he applies his own technique of study to clinical observations which have usually been made by others.

The difficulties of assessing health are well known and need not be stressed; it is the chief purpose of this paper to call attention to certain fundamental principles governing the assessment of health in childhood; and to describe the technique by which these principles are applied whether to an individual child or to a group (A). No further reference will be made to 'group' health (B).

Definitions and standards

What do we understand by the word 'health'? The Concise Oxford Dictionary defines 'health' as 'soundness of body'. Though we need not find fault with the word 'soundness', but might, if preferred, substitute 'wholeness' or 'well-being' for it, we cannot limit our definition to 'body'; the child, like the adult, is an individual who possesses mind and spirit as well as body; to be healthy he must be sound in all respects. Furthermore, health ('ease' of mind, body and spirit) is a positive, dynamic term, and we must train ourselves to look for positive indications, both structural and functional, of its presence, and not to rest satisfied with the absence of signs of dis-ease ('negative' health).

What standards are we to adopt? For children we cannot set our standards too high, though 'maximum' is not always the most suitable adjective by which to describe the ideal, e.g. for features such as height and weight. Generally speaking 'optimum' is a preferable word in respect both of structural (anatomical) and functional (physiological) characteristics; for it stresses the quality of standard towards which the mind of the examiner should be turning though it does not, unfortunately, give an exact description of the standard itself. On this point, to which some further reference will be made later, it should be noted that there is a prevalent tendency to employ, through thoughtlessness or ignorance, standards which are patently suboptimal. For instance, comparison of a group of 'healthy' (so-called) children of lower middle-class status with a corresponding group of children attending a private preparatory or public school reveals differences, e.g. in weight, height, bony and muscular development, posture, mental alertness and ability, which leave no doubt that the general soundness of the former group is inferior to that of the latter group. The doctor whose work is limited to children of a particular grade or status may be unconsciously handicapped in his conclusions because his standards are debased; and the administrative medical officer, dealing with average rather than optimum standards, may present to the public a report which paints the picture in unjustifiably

* Based upon a lecture given to the Medical Officers of Schools Association.

rosy colours. Average standards are sometimes helpful but often dangerous unless accompanied by an explanatory note to make their nature clear.

Some may ask whether it is possible to draw up optimum standards applicable, without variation, to each of the children composing a group. To the clinician it seems apparent that individual peculiarities consequent upon normal hereditary influences must necessarily complicate the task of arriving at agreed (optimum) standards.

Upon what evidence is the assessment of health to be made?

Following the usual practice in clinical medicine evidence is obtained from two sources: (i) the previous history of each child, and (ii) the facts elicited at clinical examination.

In regard to previous history, cognizance must be taken of the factors, both hereditary and environmental, which have been operating towards and against health, and of the developmental progress and performance of the child. By a review of the past we shall be helped in assessing the present and forecasting the future. Admittedly it is sometimes impossible to obtain a satisfactory history, even when the parents attend for the purpose; in any case the task is time-consuming. But a diligent and patient attempt should be made, for otherwise the examiner's opinion has to be based solely upon his observations at a single examination. One might as well attempt to form an opinion of a tennis player's competence by studying a single photographic exposure cut from a film of the player in action.

Whilst it is advisable that the clinical examination should include tests of functional efficiency as well as a survey of the child's structural soundness, a careful history may make a valuable additional contribution to this important (physiological) aspect of the child's health. In eliciting this history help will be obtained by bearing in mind the points described below.

What are the chief factors influencing health in childhood?

These factors, when favourable, may be described as the 'foundations of good health in childhood'. They are:—

(i) HEALTHINESS OF THE PARENTS. This includes the hereditary transmission of either beneficial or harmful characteristics; the state of the mother's health (physical and mental) during pregnancy; the financial circumstances, diet, working and living conditions of the mother during pregnancy; and the duration of the pregnancy.

(ii) THE CHARACTER OF THE CHILD'S BIRTH AND THE STATE OF HIS HEALTH DURING THE NEONATAL PERIOD. In this connexion the history may provide valuable information upon the baby's weight at birth; the presence or absence of birth-injury, respiratory difficulties, jaundice, and neonatal disease.

(iii) A SUITABLE DIET. The financial status of the parents again needs consideration; as also their housing condition, employment, and state of intelligence. One wants to know if the child was breast-fed, and for what period, and if the mother's health, hygiene and diet during lactation were favourable. The subsequent diet given to the child requires careful consideration, particularly in respect of total quantity, variety, vitamin and iron content.

(iv) HEALTHY HYGIENE AND MANAGEMENT. One may have to rely upon general impressions based upon evidence noted above. To the child housing conditions, clothing, the care of the skin, and opportunities for sound sleep and for exercise in fresh air and sunlight are of much greater importance than to the adult.

(v) A SAFE, COMFORTABLE AND PEACEFUL HOME. Under this heading should be considered not only the physical advantages of a well-ordered, comfortable home, but also that other kind of safety or security (mental and spiritual) which is enjoyed by those children whose parents are happily married and are living together in a state of concord and mutual respect. The loss of this sense of security, though obviously not understandable by the child, may have serious effects upon his nervous system, and through this upon his bodily health.

(vi) TRAINING IN THE FORMATION OF GOOD AND REGULAR HABITS. This training, e.g. in regard to sleep, feeding, plan of life in general, and control of the sphincters—when given by sensible parents and without undue emphasis or displays of emotion—promotes the child's general health and sows the seeds of self-reliance and well-ordered discipline. Many parents fail to realize how important a part the simple events of a child's life may be caused to play in promoting stability of the nervous system and in fostering the formation of robust character and attractive personality.

(vii) THE STIMULUS OF GOOD EXAMPLE. Parents of sound nervous stability, who are at one and the same time sympathetic, understanding and firm, give to their children the advantages of leadership and example which are the stronger for being founded on affection. Without these advantages children frequently become highly strung, unbalanced, undisciplined, and unhappy; their general health is sub-optimal.

(viii) OPPORTUNITIES FOR SELF-EXPRESSION AND DEVELOPMENT (PHYSICAL, INTELLECTUAL AND MORAL). Without these opportunities, wisely guided by unselfish parents, the child's body and spirit fails to expand and is liable to be stunted and distorted. In some cases ignorance or apathy of the parents may be responsible; in others the home conditions leave much to be desired; in others it is a case of unwise and sometimes selfish over-protection which, in sparing the child the pin-pricks of his early years, deprive him of the ability and strength with which to meet the greater trials of manhood. Under these and similar circumstances full health is not attained.

(ix) FREEDOM FROM INFECTION AND DISEASE. It is

unlikely that complete freedom is attainable; the history of previous illnesses will be some indication to the examiner about possible sequelae.

After obtaining as much evidence as possible regarding the influence of the factors noted above, questions should be asked about the child's sleep, appetite, vitality and temperament. The approximate dates of certain attainments (sitting unsupported, walking, speaking) should be recorded.

What can we learn of a child's general health or soundness by clinical examination?

A careful clinical examination should be made under suitable conditions, i.e. in a warm room provided with a wash-handbasin, couch, weighing machine and height scale, and the necessary instruments. The examiner should train himself to make an active search not only for the features of disease but also for the positive signs of health, as detailed below. An experienced clinician who follows this plan and considers his findings alongside the previous history may justifiably claim that his overhaul of the child will furnish a reliable picture of the state of health. But the clinician must be prepared, when need arises, to seek the help of specialists, e.g. in regard to dental health; health of the eyes and ears; mental health; nutritional status. It must, however, be emphasized that these detailed studies, although individually important, are isolated parts of the whole, and ultimately it is the health of the complete individual—a complex, composite, living unit—that has to be weighed in the balance.

The following details should be noted during routine clinical examination; and in doing so it must be remembered that allowance may need to be made for climatic conditions and other environmental influences, and for the reaction of the child to the examination itself; e.g. on a cold day a child may look paler than usual, especially if he does not know the examiner and is feeling nervous.

WEIGHT AND HEIGHT. The weight should be recorded with the child in a light garment (knickers or underpants) only, and a succession of recordings at intervals is more valuable than a single result. The accuracy of the weighing machine should be checked regularly by one of the firms who undertake this service.

GENERAL INSPECTION. The child, wearing the light garment noted above, should be seen standing at ease and then walking and running. The following features characterize a large proportion of healthy children:—

(1) The mucous membranes (e.g. the lips and palpebral conjunctiva) are definitely pink in colour.
(2) The facial expression is happy, often radiant; smiling is frequent, and the eyes are bright and responsive.
(3) The skin is smooth, elastic, and covers a sufficient layer of subcutaneous fat to give the limbs a rounded appearance.
(4) The tissue-turgor is normal.
(5) The muscles are well formed, and their tone is good.
(6) The limb-bones are almost straight.
(7) The stance is well balanced, erect, and graceful.
(8) The spine is straight and the shoulder-girdles do not drop.
(9) The arches of the feet are well formed.
(10) The movements of limbs and body, in walking and running, are characterized by elasticity, agility, vigour and poise.

Then follows the usual routine examination of the various systems, including inspection of eyes, ear-drums, mouth, tongue, teeth and throat, skin (including scalp) and urine. The abdomen should be examined by palpation while the child is lying down; the genitals should be examined at the same time. When there is some doubt regarding the significance of clinical signs (e.g. a trace of protein in the urine) it may be necessary to repeat the examination and to arrange for special tests.

At this point it may be asked whether routine clinical examination on the above lines can be regarded as a complete and adequate test of a child's health. If we are to insist upon the use of optimum standards the answer must be in the negative, because relatively slight deviations from the full normal may not be demonstrable without the assistance of the specialist. For instance, a minor error of refraction, or an 'island' of deafness, although impossible of recognition by the ordinary clinical examination, may have some influence upon posture, or may hinder the child's full development in the mental and intellectual spheres; and even if these secondary effects were recognized by an astute clinician, he would still require the help of specialist colleagues to unmask the cause. Before a general rule could be formulated upon this difficult question, the possible disadvantages of more searching examination, such as expense and the fear of inducing neurosis in both parents and child, would require consideration. Educated lay people are now sufficiently enlightened regarding the preservation of health as to take their children for periodic dental examination, followed by conservative treatment when necessary, and it seems probable that both medical and public opinion will develop along similar lines in regard to other aspects of full health. For instance, the educational psychologist is likely to play an increasingly important part in recognizing and advising upon deviations from full health, such as occur with special frequency in categories (v) to (viii) on p. 53 ('foundations of good health'). At the same time it may be claimed that an experienced paediatrician is competent to recognize those children who are in need of psychological or psychiatric examination, provided that he has sufficient time to take a detailed history and to study the child carefully; and the same holds good in regard to other forms of specialist examination which might be necessary. It would be at variance with sound practice if a situation were to develop in which children were given merely a perfunctory general

medical examination prior to visiting a number of specialists.

General comments

(With special reference to the assessment of 'Group' health A)

The following observations are based upon the statements and views expressed above; they include the gist of a short memorandum on the routine medical inspection of school children which was drawn up by the British Paediatric Association in response to an inquiry by the Ministry of Education.

1. There can be few kinds of medical service more valuable to the welfare of the community than that of a school medical officer, provided that he (or she) is a keen practitioner who is adequately qualified to interpret and perform his duties and who can rely upon the co-operation and support of those with whom his work brings him into contact, especially his senior medical officers, the school teachers and the parents.

2. The school medical officer, whether a general practitioner or a whole-time public health officer, should have had paediatric training, and should hold the Diploma in Child Health. He should be attached, whenever possible, to a University Department of Child Health, or to a recognized Children's Hospital, or Children's Department of a recognized General Hospital. In this way he would be able to maintain contact with clinical paediatrics in a centre where teaching and research work are in progress; and the conditions of his employment should encourage him to do this. Even an enthusiastic doctor loses heart and zest when he is bound to a routine which soon becomes monotonous. The more experienced the practitioner the better does he recognize and understand the various constitutions, temperaments, outward appearances and functional capacities of the children before him, and the wiser he is in avoiding the danger of accepting sub-optimal standards.

3. The services of a paediatric consultant should be available to each Education Authority, to give advice upon cases referred to him and upon special problems which may arise.

4. The views of the British Paediatric Association regarding the duties of a school medical officer may be quoted in full:—

'He should be a medical officer to a group of schools and be responsible for the health of all the children while at school, and act, in fact, as a member of the school staff. He should superintend the general hygiene of the school, including sanitation and diet, and deal with epidemics. He should interview parents and take every opportunity of acquiring knowledge of the child's family background. He should teach older children in personal hygiene and the maintenance of health.

'He should be free to visit the school at any time and be encouraged to make investigations into any problems that might arise. In this way he would become known to the pupils and the pupils to him. During holiday times he could visit the hospitals or attend post-graduate study classes, and engage in research and investigations, some of which would be possible from his own records.'

To this it may be added that he should advise on the physical education of the children and he should maintain a close liaison with the school-teachers, particularly those who are concerned with physical education.

5. The school medical officer must have adequate time to enable him to carry out the medical inspections with care, and to hold interviews with parents and discussions with school-teachers. At the first examination an average of 15 minutes should be allowed for each child.

6. A suitably equipped and warm consulting room should be provided for the doctor's use in the school buildings, and adjacent rooms for the undressing of children and testing of urines.

A trained nurse who holds the certificate of Sick Children's Nurses should be present to give general assistance, including the recording of weight and height and testing of urines. If she also takes the history her notes should be checked, and where necessary amplified by the doctor during his interview with the parents.

7. Parents should be encouraged to attend in order that a reliable medical history may be available, and advice and encouragement given to them.

8. The record chart should be carefully drawn up, and should provide the doctor with space sufficient to enable him to keep careful notes not only of routine observations but also of particular aspects of child health which seem to offer useful prospects of adding to knowledge. Care should be exercised in regard to the terminology used; in the past confusion of thought has resulted from the use of descriptive words which in fact possessed a narrower significance than was intended, e.g. 'state of nutrition', or 'nutrition' to signify 'state of health in general'.

9. Suitable arrangements will be necessary for dental examination, followed by conservative treatment when necessary, and for the various specialist examinations which may be required.

10. Every encouragement should be given to the furtherance of research into the problems of assessing and preserving health in childhood; for instance, the wider application of so-called 'screening' methods in regard to nutrition, hearing, vision, mental health; the more intelligent use of physical exercises; and the relationship of physical and mental health to educational progress.

THE EFFECT OF NATIONAL BREAD, OF IRON MEDICATED BREAD, AND OF IRON COOKING UTENSILS ON THE HAEMOGLOBIN LEVEL OF CHILDREN IN WAR-TIME DAY NURSERIES

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The presence in war-time day nurseries of groups of young children provided an opportunity for investigating anaemia in children under five years of age. There are, however, considerable drawbacks to such investigations in day nurseries. Chief among these are the high rate of cross-infections, the unstable population, and the investigator's ignorance, from lack of contact with the mothers, of the children's life outside the nursery.

Aims of the investigation

The investigation was concerned with the etiology of anaemia as seen in the nurseries. The initial object was to determine whether or not a small addition of iron to the children's bread, made from 85 per cent. extraction flour, would produce a rise in haemoglobin level. If this fortification proved effective, it might be a valuable means of ensuring a sufficient supply of iron to the general population, and might provide evidence regarding the normal mean haemoglobin level in children of pre-school age. White bread 'fortified' with iron (4 to 16 mgm. Fe in each pound) and other substances is in wide use in the United States (Tobey, 1942; Editorial, *J. Amer. med. Ass.*, 1945), but no evidence appears to exist as to the influence on health of iron medication in this form. Observations were also made on the influence of national bread, without medication, and of iron cooking utensils on the haemoglobin level. The haemoglobin level of the children in the nurseries was compared with mean values obtained about a year earlier of children attending welfare centres. Changes in haemoglobin level in the nurseries and the effect of diet and of drug therapy will be dealt with in another article.

Technique of haemoglobin estimation

The blood was taken from a prick in the heel with a cutting needle after the foot had been warmed in hot water. Though the foot was always warmed it proved impossible always to ensure a warm leg, and this or resistance and crying on the part of a child probably produced fallacious values in individual cases. Three different observers made the estimations, but all estimations at any one nursery were made by the same observer. All estimations were made with a Haldane colour tube, and the same colour tube and set of diluting tubes were used at all the nurseries. Figures given have had the National Physical Laboratory correction factor applied for colour tube and pipettes, and a mean percentage correction factor for the diluting tubes. This percentage correction was necessary because the distance between the 20 and 140 marks, and hence the diameter of the diluting tubes, differed from the B.S.I. standard. The National Physical Laboratory provided further small corrections for these diluting tubes which were obviously negligible and were omitted. At 80 per cent. the mean of the corrections omitted was −0·3 and the maximum individual correction ignored was −0·9.

Clinical material

The children were aged six months to five years, and attended one or other of three day nurseries in Islington, in north London. The nurseries, which we will call A, B and C could accommodate 55, 66 and 33 children respectively, or 154 in all. They were open from 7 a.m. to 7 p.m. on six days weekly. The mothers, in addition to their home duties, were engaged on work outside their own homes, and, with few exceptions, this outside work was full time. They included factory hands, railway porters, bus conductors, with some shop assistants, canteen workers and nursery workers. A few were engaged in clerical work. Breakfast, dinner and tea were supplied in the nurseries, but some children, varying from about a quarter to half the total number, had breakfast at home and no breakfast at the nursery. Probably all children had a meal at home at night

after their 3.30 p.m. nursery tea, and most had some food before arrival. As the mothers kept the children's ration books, it was possible for them to give rationed food at home: to what extent this was done is unknown. At each of the three nurseries A, B and C, the children were divided into two groups, as nearly as possible equal as regards haemoglobin level, age, sex and incidence of infected tonsils or bronchitis at the time of starting treatment, and one group received medicated bread and the other acted as a control. No iron medication other than that provided in the iron-fortified bread was given in these nurseries. The number of children finally available for comparison in this part of the investigation was 138, out of a total of 197 examined during August, 1942, to February, 1943.

Haemoglobin level by age at beginning of observation compared with the haemoglobin level of a group of children attending welfare centres

The mean initial haemoglobin level of the nursery children aged one to two years averaged somewhat lower than that of those aged six to twelve months (table 1). Thereafter there was a fairly steady increase in haemoglobin level with each year of life up to five years of age, when the children left to attend school. These trends were fairly consistent at each of the three nurseries and the rise with age was much steeper than in the groups of children of school age examined by us. The mean figure for all three nurseries at one to two years old was 73·2 per cent. and at four to five years 85·5 per cent., a rise of 12 per cent. in three years, or an average rise of 4 per cent. per year, in contrast with about 1·4 per cent. yearly rise which we found in school children between the ages of seven and eleven years (Dobbs et al., 1944). Though the mean haemoglobin values at nursery B were slightly lower than at the other two nurseries, this may well have been due in the main to a difference in colour matching. The estimations at nursery A were made by H.M.M.M. and those at nursery B by K.B. K.B., in a series of ten test colour matchings (conducted by Dr. R. G. Macfarlane for the Haemoglobin Survey Committee of the Medical Research Council), gave readings averaging approximately 2 per cent. lower than H.M.M.M.'s matchings on the same series. This difference in colour matching, if consistent, would almost balance the mean difference in readings at nurseries A and B. R.H.D. made the estimations at nursery C until the end of the present investigation in February, 1943, but he did not take part in this colour-matching test as he was by then in the army. Table 1 includes, for the sake of comparison, haemoglobin values (corrected as already indicated in this paper) for children of similar age examined at welfare centres in 1941 (Wills, Mackay, Bingham and Dobbs, 1942). These had at each age over twelve months a higher mean haemoglobin level than any of the present three nursery groups at the outset of the investigation. The differences varied at different ages between about 3·5 and 5·5 per cent. above the mean for the two nurseries examined by the same two observers who made the estimations on nearly all the welfare children. Since these differences are consistent, and appear in every small subdivision, it may fairly be assumed to be a real difference and not due to chance, in spite of the fact that the difference in haemoglobin level between each age group at nurseries A and C, as compared with the corresponding group at the welfare centres, is sometimes more and sometimes less than twice its standard error.

Other nursery children examined in 1941, like those in the present series, had a mean haemoglobin level lower than this welfare group.

TABLE 1

HAEMOGLOBIN LEVEL BY AGE AT BEGINNING OF OBSERVATION IN AUGUST AND SEPTEMBER, 1942

Group	Estimated by	No.	6 m.–12 m.		1–2 yr.		2–3 yr.		3–4 yr.		4–5 yr.	
			Mean Hb.	No.	Mean Hb.	No.	Mean Hb.	No.	Mean Hb.	No.	Mean Hb.	No.
Present series, 1942—												
Nursery A	H.M.M.M.	55	75·8	4	75·6	13	79·8	15	82·2	10	86·1	13
Nursery B	K.B.	47	72·4	2	71·0	10	76·7	15	81·0	15	83·8	5
Nursery C	R.H.D.	31	85·6	4	71·9	8	83·1	9	88·0	6	85·9	4
Nurseries A, B and C ..		133	79·0	10	73·2	31	79·4	39	82·7	31	85·5	22
Nurseries A and C ..	H.M.M.M.	86	80·6	8	74·2	21	81·0	24	84·3	16	86·0	17
Standard deviation ..	and R.H.D.	—	6·42	—	8·77	—	8·17	—	5·74	—	4·45	—
Series examined in 1941 at Welfare Centres	H.M.M.M.	164	79·5	52	79·4	49	84·7	32	89·0	21	91·4	10
Standard deviation ..	and R.H.D.	—	8·38	—	8·59	—	7·89	—	7·04	—	8·74	—
Difference: Mean Hb. of Welfare Centre Series less mean of Nurseries A and C		—	−1·13	—	+5·21	—	+3·70	—	+4·69	—	+5·40	—
S.E. of difference ..		—	2·55	—	2·25	—	2·17	—	2·10	—	2·97	—

Medicated bread

At each nursery one group received National bread made of 85 per cent. extraction flour, the other group received the same National bread with an addition of ferrous carbonate to provide an additional 7 mgm. of Fe in each ounce of bread. The ferrous carbonate was incorporated in the common salt habitually added in making the bread. We are indebted to Dr. R. A. McCance and Miss E. M. Widdowson for help and advice about this 'fortification' of the loaf, as it is called in the United States. The writers mistakenly assumed that by the summer of 1942 all flour used in bakeries had an addition of calcium carbonate, and it was impossible at the end of the period of observation to find out which batches had been so treated, as the flour was derived from many sources. By Christmas 1942, i.e. approximately half-way through the investigation, about half the bread in the country, according to information available, was being fortified with calcium, and the proportion of bread so fortified steadily increased.

The addition of ferrous carbonate to the bread made it look slightly darker than unmedicated bread, but since the difference was slight, direct comparison was necessary to be sure of the colour difference. The taste was scarcely affected, and the two breads could not be distinguished by taste with any certainty even on direct comparison. The addition of ferrous sulphate, in the same quantity, gave the bread a slightly greenish-grey appearance, hence this salt was considered unsuitable for the purpose of the investigation.

Quantity of bread consumed and the increase in iron intake provided by medication of the bread. Bread, in some form, was usually provided at breakfast and tea in the nurseries. The average daily intake was estimated by weighing, at each meal for one week, all the bread consumed by the children over one year old at two nurseries. All children received National bread, and ate during the week an average of 2 to 3 ounces daily per head for all ages between one and five years, whether or not the bread contained the added ferrous carbonate. The estimate was a rough one and the intake varied widely on different days of the week, depending in part on what other cereal foods were provided. On different days of the week the average consumption per head in the group aged one to two years varied between $\frac{3}{4}$ and $4\frac{3}{4}$ ounces and in the group aged three-and-a-half to five years it varied between 2 and $5\frac{1}{2}$ ounces. Hence, on different days of the week, the amount of iron derived from the addition of ferrous carbonate to the bread varied from about 5 to 33 mgm. of Fe per head for children aged one to two-and-a-half years, and from 14 to 38 mgm. per head for those aged three-and-a-half to five years. Children of all ages between one and five years having breakfast and tea in the nursery received an average addition of 20 mgm. of Fe per head per day; those having tea only received about 14 mgm. daily. Thus far more iron was provided than could possibly have been derived from unmedicated food alone. In the particular week when the estimate of bread intake was made the smaller children at nursery A ate a good deal more bread than the corresponding age group at nursery B.

Effect of medicated bread. The observation with medicated bread continued for five months until February, 1943, and haemoglobin estimations were repeated at intervals of four to six weeks during this period. At each nursery the children receiving the medicated bread and their controls had similar haemoglobin levels throughout the five months (tables 2 and 3). The small differences in mean haemoglobin level between the medicated children and the controls are obviously due to the small numbers in each group. The medicated bread had, therefore, no influence on the haemoglobin level. The percentage of days missed by children having medicated bread and by controls was also almost identical, namely 25 per cent. (calculated to the nearest whole number) of total possible attendances. This figure applies to the absences at the two largest nurseries combined (see table 5).

Effect of National bread

The National bread was made from 85 per cent. extraction flour; from March, 1942, the law required that not less than 75 per cent. of the flour in bread must be of 85 per cent. extraction. The consumption of National bread was without any effect on the

TABLE 2

HAEMOGLOBIN LEVEL OF CHILDREN RECEIVING IRON MEDICATED BREAD AND NATIONAL BREAD—ALL AVAILABLE CHILDREN

		1942 Aug. and Sept.		Oct.		Nov.		1943 Jan.		Feb.	
		Mean Hb.	No.	Mean Hb.	No.	Mean Hb.	No.	Mean Hb.	No.	Mean Hb.	No.
Nursery A.	Medicated bread	80·2	30	81·9	27	86·8	27	86·2	18	89·6	23
	National bread	80·8	25	84·0	27	86·2	25	87·7	15	88·5	16
Nursery B.	Medicated bread	78·7	24	78·9	25	80·8	17	—	—	77·8	20
	National bread	76·2	23	78·5	27	78·4	20	—	—	77·9	18
Nursery C.	Medicated bread	81·5	16	83·3	15	77·7	9	79·9	9	81·9	11
	National bread	82·2	15	81·5	13	77·9	11	80·8	6	79·7	9

haemoglobin level at nurseries B and C where the mean haemoglobin of children having the National bread, whether medicated or not, remained almost unchanged for five months. The mean haemoglobin level of children at nursery A rose by about 8½ per cent. in five months, but, as the National bread was without effect on the haemoglobin level in the other two nurseries, it is difficult to suppose that the rise can be attributed to the bread.

TABLE 3

HAEMOGLOBIN LEVEL OF CHILDREN RECEIVING IRON MEDICATED BREAD AND NATIONAL BREAD—CHILDREN WHO WERE EXAMINED IN AUGUST OR SEPTEMBER, 1942, AND RE-EXAMINED IN JANUARY OR FEBRUARY, 1943

	1942 Aug. or Sept.		1943 Jan. or Feb.		Difference between first and last estimate
	Mean Hb.	No.	Mean Hb.	No.	
Nursery A—					
Medicated bread..	80·0	26	89·3	24	+8·9
National bread ..	80·3	14	89·2	14	+8·9
Nursery B—					
Medicated bread..	80·6	17	78·9	17	−1·7
National bread ..	77·3	15	78·8	15	+1·5
Nursery C—					
Medicated bread..	83·9	12	80·3	12	−3·6
National bread ..	79·7	11	80·0	11	+0·3

Morbidity rate and haemoglobin level

The steady rise in haemoglobin at nursery A in the autumn and winter of 1942–43 (tables 2 and 4) was present in each age group and in almost every child in the group. The rise could not have been due to any muddle whereby controls received the medicated bread, since the results in the other nurseries over the same period showed that the medicated bread was without effect on the haemoglobin level.

A difference in morbidity rate as a possible explanation of this difference in haemoglobin level needed investigation. A record was kept by the matron and sister at each nursery of the absences of each child, with, if known, the cause of absence.

TABLE 4

HAEMOGLOBIN LEVEL OF CHILDREN AT NURSERY A COMPARED WITH THAT AT NURSERIES B AND C—CHILDREN ON MEDICATED BREAD AND ON NATIONAL BREAD COMBINED

	1942, Aug. and Sept.			1943, Feb.			Final mean less initial mean	
	Mean Hb.	S.D.	No. of children	Mean Hb.	S.D.	No. of children	Diff.	S.E. of diff.
Nursery A	80·4	7·90	55	89·2	5·59	39	+8·8	1·39
Nursery B	77·4	7·32	47	77·9	6·94	38	+0·5	1·55
Nursery C	81·8	8·81	31	80·9	7·26	20	−0·9	2·27

The great majority of absences were due to illness of the child, but children were also kept away on account of quarantine for contact with an infectious illness, illness of the mother, or return on leave of a father in the Forces. The rules for exclusion on account of contact with infection were identical at all the nurseries. Hence the absence rate is not strictly an index of the morbidity rate of the children but, in view of possible differences in recording at different nurseries, it seemed the best index available. Therefore periods of absence, irrespective of cause, were compared. Many children ceased attendance altogether after developing an illness. As approximately the same proportion of children in each nursery left because of illness, a child ceasing attendance for good after, for example, developing measles, ceased to be reckoned as a member of his group from the day of his last attendance, though, of course, this involved an underestimate of the child's total period of illness. The incidence of infections, particularly respiratory tract infections, was high, often nearly every child in the nursery had a running nose, and one cold followed close on the heels of another. Children were not excluded for colds in the head.

Table 5 shows the percentage of days missed by the children at the two larger nurseries and their

TABLE 5

PERCENTAGE OF DAYS ABSENT AND HAEMOGLOBIN LEVELS AT NURSERY A AND NURSERY B

Nursery	Aug. and Sept. 1942 Mean Hb.	Sept. 21–Nov. 15, 1942			Nov. 1942 Mean Hb.	Nov. 15, 1942–March 5, 1943			Feb. 1943 Mean Hb.	Sept. 21, 1942–March 5, 1943			Sept. 21, 1942–March 5, 1943 Days absent as per cent. of total possible attendance	
		Possible attendance	Absences			Possible attendance	Absences			Possible attendance	Absences		Children on National bread	Children on Medicated bread
		Days	Days	Per cent.		Days	Days	Per cent.		Days	Days	Per cent.		
A	80·4	3208	504	15·7	86·6	5346	1412	26·4	89·2	8554	1916	22·4	24·9	25·3
B	77·4	3268	551	16·9	79·5	5819	1969	33·8	77·9	9087	2520	27·7		

haemoglobin levels. Between September, 1942 and March, 1943, i.e. during the whole period of this observation, the children at nursery B, where the haemoglobin level was stationary, were absent for 28 per cent. of their possible total attendance; those at nursery A, where the haemoglobin level rose, for 22 per cent. However, the main rise in haemoglobin level at nursery A occurred before the middle of November and the main difference in the absence rates occurred after the middle of November; from September to the middle of November the absence rates were roughly similar, the percentage of days missed at nursery A being 15·7 and nursery C 16·9. By November the mean haemoglobin level at nursery A was already about 7½ per cent. higher than at nursery B in spite of the very small difference in the morbidity rates up to that date. Thus the difference in morbidity rate followed the improved haemoglobin level at nursery A. The lower morbidity rate at nursery A may have resulted from the higher haemoglobin level but did not cause it. It is, of course, arguable that the types of infection at the two nurseries differed in their effect on haemoglobin level, but there is no evidence that infections were of a more severe type at nursery B during the period in question.

Iron cooking utensils and iron intake

It has been suggested that iron cooking utensils may have provided an important source of dietary iron for our ancestors in past centuries. The present investigation offered an opportunity for examining the effect of iron cooking vessels on the iron intake of these small children. At nursery A, where the children showed a rise in haemoglobin level in the autumn and winter of 1942–43, more cooking was done in iron utensils than at the other two nurseries, and some of the enamelled saucepans were considerably chipped, exposing the iron base. Hence possible gross 'contamination' or 'fortification' of the food from this source was next investigated. Thanks are due to Dr. R. A. McCance and Miss E. M. Widdowson for their generous help and the large amount of time they gave to estimating the degree of iron contamination due to the various cooking vessels used. Table 6 shows that apple cooked in an aluminium saucepan contained 0·19 mgm. of iron per 100 gm.; cooked in the polished iron saucepan used for fruit at nursery A, the iron content was increased fifteenfold; cooked in an old-fashioned heavy black iron saucepan at nursery B it was increased fivefold. During the latter part of 1942, while the investigation was in progress, apples were frequently provided at the nurseries, but at nursery B they were given raw 'when possible', whereas at nursery A cooked apple was regularly given. Potato, not being acid, showed little iron contamination during cooking. At nursery A a stock pot was in daily and constant use and the stock received prolonged cooking each day, first in a polished iron saucepan, from which it was transferred to a chipped enamel one for further cooking. At nursery B the stock was cooked in an aluminium pot and the particular sample examined contained only about one-nineteenth of the quantity of iron found in the sample from nursery A. It is not, however, known what were the original ingredients or the initial iron content of either sample of stock.

TABLE 6

EFFECT OF IRON COOKING UTENSILS ON IRON CONTENT OF FOOD (MISS E. M. WIDDOWSON)

Foodstuff	Nursery	Cooking utensil	Fe mgm. per 100 gm.
Apple	Nursery A	Aluminium	0·19
		Polished iron *	2·88*
		Chipped enamel	0·52
	Nursery B	Iron, blackened *	0·99*
Potato	Nursery A	Aluminium	0·40
		Chipped enamel *	0·52*
	Nursery B	Aluminium *	0·58*
		Polished iron	0·46
Stock	Nursery A	Polished iron	1·77
		Polished iron→chipped enamel *	2·67*†
	Nursery B	Aluminium *	0·14*†

* Usual cooking utensil for foodstuff concerned at this nursery.

† Original ingredients of stock not the same.

It seemed, therefore, that iron cooking utensils might account for the rising haemoglobin level at nursery A, and, if so, this would be a really important finding. However, further investigation did not bear this out.

A comparison was made of the iron content (exclusive of the iron that derived from medication of the bread) of one week's food intake of children between two and three-and-a-half years old at nursery A and at nursery B respectively. Unfortunately the iron intake was estimated when the medicated bread investigation was over and the figures in table 7 cannot be taken as indicating the

TABLE 7

IRON CONTENT OF DIET IN MILLIGRAMMES CHILDREN AGED 2–3½ YEARS

Date 1943	Nursery A		Nursery B		Comments
	Fe in 6 days	Fe per day	Fe in 6 days	Fe per day	
May 24–May 30	23·2	3·9	—	—	Diet included scarcely any fruit.
May 31..	—	—	—	—	Diet improved at all nurseries.
June 2–June 9	—	—	34·6	5·8	Diet included scarcely any fruit
Aug. 28–Sept. 3	24·4	4·1	—	—	A little cooked fruit given daily.
Sept. 4–Sept. 10	—	—	26·7	4·4	A little cooked fruit given daily.

relative iron intake at the two nurseries between August, 1942, and February, 1943, when the investigation was in progress. Unknown to the authors, considerable changes and improvements in all the nursery diets were instituted from May 31, 1943, onwards. At nursery A the first week's collection of food was before the improvement of the diet and at nursery B the first collection of food was just after the change in feeding, so that unfortunately no comparison is possible of the iron intake from natural sources during the period covered by the haemoglobin estimations set out in tables 2 and 3. Since acid foods are most likely to take up iron on cooking, it would be in the fruit season that augmentation of the iron intake from cooking vessels made of this metal would be most marked. Hence if a difference in cooking utensils caused the rising haemoglobin level at nursery A, then in the fruit season the iron content of the diet at that nursery should be materially higher than that at nursery B. In May or June, 1943, and again in the fruit season in August and September, 1943, samples of food as nearly as possible the same as the actual intake of an individual child were collected by one of us at each meal daily for a week and the samples pooled. A different child was chosen at random at each meal. When the child was on medicated bread, plain National bread was substituted in the sample. During the test weeks in August and September, 1943, cooked fruit was given daily; the fruit helpings, however, were small, e.g. one small plum or an equivalent bulk of apple. The result of the analysis was disappointing. In both weeks the iron intake was greater at nursery B where there was less cooking in iron vessels. The conclusion follows that there cannot have been any gross iron contamination of the food at nursery A from cooking utensils, and the use of iron cooking utensils at the nursery would not influence the haemoglobin level. This seems a legitimate conclusion in spite of the fact that the iron content of the diet at nursery B during the autumn and winter of 1942–43 was probably distinctly lower than it was at the dates of the iron analyses, by which time the diet had been improved. Since neither morbidity rate nor the type of cooking utensils in use provided an explanation of the difference in haemoglobin level at nurseries A and B by the end of 1942, it is probable that it was the result of a better diet at nursery A, but the data available as to the diets at this period are very incomplete.

Discussion

The beneficial effect of any line of treatment can only be shown on a group of persons who are subnormal and hence it is necessary to know whether or not these nursery children were anaemic at the outset of the investigation. The normal mean haemoglobin level for children of six to twelve months is not less than 86 per cent. (Mackay, 1933), but the normal mean level in children after the age of infancy is not known, still less the range of the normal. There is no doubt, however, that the mean initial haemoglobin level in these nursery children was subnormal. This is shown (1) by the fact that the mean initial haemoglobin values of the nursery children at each year of age were consistently lower than those of children examined at welfare centres in 1941 (moreover there is reason to suppose that this welfare group itself included many children with subnormal haemoglobin levels), and (2) by the rise in mean haemoglobin level at all the nurseries during 1942–44, which it is hoped to discuss in another paper.

It has been suggested that consumption of National bread with a considerably higher iron content than white bread has had a beneficial effect on haemoglobin levels in this country (Davidson et al., 1944a and b). At nurseries B and C, the haemoglobin level, though subnormal, remained stationary in spite of the consumption of 2 to 3 ounces daily of National bread. This result is in accordance with the metabolic observations published by Widdowson and McCance (1942) showing the poor absorption by the human subject of iron from bread made of flour of high extraction.

The type of anaemia common in this country in babies and young children, particularly those aged six months to three years, has been shown by many workers to respond to iron therapy (Mackay and Goodfellow, 1931; Parsons and Hawksley, 1933; Davidson and Fullerton, 1938), and is commonly accepted as an iron deficiency anaemia, though the deficiency of iron may be conditioned by other factors. As there seemed no reason to suppose the anaemia at the nurseries was of a different type, a therapeutic effect from the iron medicated bread was expected. The expected rise in haemoglobin did not occur. This fact might be due to any one of several causes, e.g. (1) that the anaemia was not an iron deficiency anaemia, (2) that the high incidence of intercurrent illness prevented response to iron, (3) that the dose was inadequate, (4) that the iron was precipitated by the phytic acid in the bread and consequently not absorbed.

The effect of a liberal dose of iron in the form of a mixture has been tested in the nurseries, and a rise in haemoglobin, albeit a small one, was obtained. (These results await further analysis.)

Various factors, known and unknown, influence the degree of absorption of iron and its utilization in haemoglobin building. One of these is certainly infection (Mackay and Goodfellow, 1931; Parsons and Hawksley, 1933) and the morbidity rate at the nurseries was high. Fullerton (1937) found in the children of a residential nursery, as a result of infections in the late winter and spring months, actually a considerable drop in haemoglobin level in spite of iron medication, but when health improved in the summer haemoglobin rose with iron treatment. There is thus every reason to suppose that in these nurseries too illness would retard a rise in haemoglobin level. But it seems improbable that illness was sufficient at nursery B in the autumn of 1942 to prevent a rise in haemoglobin level which would otherwise have occurred from the con-

sumption of iron medicated bread, since a similar amount of illness did not prevent a rise in haemoglobin level in nearly every child at nursery A over this period.

As regards the size of the daily dose of iron received by the children in the medicated bread, this, though variable, was a large intake as measured by dietetic standards and a very small intake by therapeutic standards: a mean intake per head of 14 and 20 mgm. respectively for children not having and for children having breakfast at the nursery. Why the effective therapeutic dose of iron is so grossly in excess of any quantity obtainable in the food is as yet unexplained, but even allowing for the large size of the ordinary therapeutic dose, one would have expected in five months some response in case of iron deficiency anaemia from the quantity of iron given had there been no hindrance to its utilization.

There remains the possibility that 85 per cent. extraction flour is a quite unsuitable vehicle for iron medication, that iron phytate was formed and absorption was consequently very poor. Widdowson and McCance (1942) have demonstrated in the human subject the greatly reduced iron absorption from bread made from 92 per cent. extraction flour as compared with white flour on account of the insolubility of iron phytate. It is supposed that there was enough phytic acid present in 85 per cent. extraction flour to combine with much of the iron added to the bread. One of us (Mackay, 1940) has given infants soya flour (Berczeller process) in quantities to supply about 10 mgm. of iron daily for a 12 lb. baby. Most soya flour contains a considerable amount of phytic acid (McCance, personal communication). This soya feeding diminished the incidence of anaemia in infants, but did not prevent severe nutritional anaemia in a few cases, anaemia which was cured by giving full doses of iron as a drug. These findings are compatible with the view that phytic acid diminished, but did not inhibit, the utilization of the iron present. As it has not been possible to compare the relative proportion of phytic acid and of iron in the medicated bread and the soya flour used, nor the possible influence of other bases present, the reason why the iron in the soya flour was apparently better utilized than that in the bread cannot be suggested. It is of interest that Nakamura and Mitchell (1943) found that iron phytate and the iron in whole wheat was only about half as well utilized in haemoglobin building by the young rat as was the iron of ferrum redactum or sodium iron pyrophosphate, both of which are used in the fortification of white flour in the United States.

There is left the fact that fortification of the National loaf with iron, with a consequent increase of the iron content of the diet by about 14 to 20 mgm. daily, did not produce a rise in mean haemoglobin level among children with a subnormal haemoglobin level, and that the most likely cause seemed to be the presence in the bread of phytic acid. It is hoped further investigation will show whether comparable quantities of iron given in a mixture will increase the haemoglobin level.

It is an interesting fact that iron cooking utensils had little influence on the iron intake at nursery A. Though the iron saucepans in use greatly increased the iron content of stewed fruit, the quantity of cooked fruit consumed at these nurseries was so small that its influence on the total iron intake was negligible. Incidentally it is unlikely that iron cooking utensils influenced our ancestors' haemoglobin level unless they consumed large quantities of cooked fruit.

Summary and conclusions

Observations were made at three war-time day nurseries with accommodation for one hundred and fifty-four children ranging in age from six months to five years. Haemoglobin estimations were made with a Haldane haemoglobinometer at intervals of four to six weeks. The sickness rate was high and the average attendance of the children was about three out of four possible attendances over the five month period of the investigation. The mean haemoglobin level was subnormal at the outset: in infants aged six to twelve months it was about 79·0 per cent., and in infants of one to two years 73·5 per cent., with thereafter a progressive rise to 85·5 per cent. by four to five years. The mean value was lower than that of children examined at welfare centres the year before. At each nursery half the children received for five months National bread, made from 85 per cent. extraction flour, and the other half the same bread fortified with 7 mgm. iron (reckoned as Fe) per ounce, which provided the children with far more iron than they could have obtained from natural sources. The average daily intake of bread by children aged one to five years was about 2 to 3 ounces, providing about 14 to 20 mgm. of additional iron. This medicated bread was without effect on the haemoglobin level or the morbidity rate. It is suggested that the phytic acid of 85 per cent. extraction flour interfered with the utilization of the added iron. National bread made from 85 per cent. extraction flour was itself without effect on the haemoglobin level over a period of five months.

Iron cooking utensils were in use at one nursery but did not make an appreciable difference to the mean iron intake of the children as the consumption of cooked fruit was small.

Though the high incidence of infections was probably a factor influencing the haemoglobin level, it did not prevent a rise of about 8 per cent. in the mean haemoglobin level of children at nursery A between September, 1942 and February, 1943. The absentee rate during the material period was similar at nursery A and nursery B, and the rising haemoglobin level at nursery A was probably due to a better diet, but adequate data to establish this inference are lacking. This investigation supports the view that 85 per cent. extraction flour is not a good vehicle for increasing iron consumption.

Acknowledgements

The authors' sincere thanks are due to Dr. V. Freeman, Medical Officer of Health of Islington, as well as to all those who undertook much extra work in difficult times to make our investigation possible, especially to Dr. K. H. Hirst, Deputy and Acting Medical Officer of Health, to the Matrons and Staffs at the nurseries, to the pharmacists at the Queen Elizabeth Hospital for Children, to Mrs. P. Dagnall for technical assistance and to Messrs. Beales & Co., who supplied us with medicated bread. Thanks are also due to Dr. R. A. McCance and Miss E. M. Widdowson for valuable advice and for all the food analyses on which the conclusions are based.

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THE FRAGILITY OF THE RED CELL TO HYPOTONIC SALINE IN INFANCY AND CHILDHOOD

BY

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(From The Radcliffe Infirmary, Oxford)

A survey of the literature dealing with the resistance of the red blood corpuscle in infancy and childhood to hypotonic solutions of saline reveals a great divergence of opinion. Some authors (Goldbloom and Gottlieb, 1929; Cathala and Daunay, 1908; and Martha Wollstein, 1938) believe that the resistance of the red blood cell to hypotonic solutions of saline is diminished in the foetus and new-born child in comparison with what obtains in adult life; some (Mitchell, 1928) believe that there is no difference between early and adult life in this respect, whilst others again (Hornung, 1925; Whitby and Hynes, 1935; and Waugh, Marchant and Maughan, 1938) hold that the resistance is normal at birth and then increases during the first few days of life, reaching its maximum about the fourth day, after which it gradually returns to the normal adult level.

This diversity of opinion is not to be wondered at, since hardly two workers have employed the same method, and practically all have omitted to take into account factors which are now generally admitted to have a marked effect on the resistance of the red blood corpuscle.

The degree of haemolysis is determined either by noting the amount of haemoglobin liberated from the cells, or by observing the rate of disappearance of the red cells themselves. Those who practise the latter method, either by counting the number of cells in a unit volume of the mixture (Simmel, 1923; Whitby and Hynes, 1935; and Cormick, 1942) or by noting the amount of the centrifugalized deposit (Beebe and Hanley, 1935–6), dignify their particular method by calling it a ' quantitative test ' in contrast to the former which they consider merely qualitative in character. Such a distinction is untenable. All methods are qualitative in their nature, in that it is the character of the reaction to hypotonic saline which is being observed, and at the same time they are all quantitative in that the degree to which haemolysis has taken place in any particular concentration is determined, whether this be judged from the depth of the supernatant-stained fluid, from the amount of the centrifugalized sediment composed of the corpuscles still unlysed, or from the calculated number of corpuscles still clearly discernable in the various saline concentrations. The fact that a progressive increase in the process, with a fall in the saline concentration, is revealed by all methods surely demonstrates the quantitative nature of all the tests. There might be some justification for a claim that the different methods of detecting the process of haemolysis are not equally sensitive or equally exact, but that is not to suggest that any of them do not reveal the severity of the process relative to the degree of hypotonicity of the saline solution mixed with the blood. It is easier to detect slight changes in colour, particularly when dealing with lighter shades when differences of as small as 2 per cent. are easily appreciated than it is to detect slight differences in the numbers of red cells suspended in the fluid. Those familiar with routine blood counts are well aware that greater variations from day to day, and even in different specimens taken at the same time, are found in the red cell estimations than in those of the haemoglobin. Hence it would appear that the so-called **qualitative** test is the more accurate and more useful from a **quantitative** standpoint. These facts would seem to be of particular significance in deciding on the point at which haemolysis begins and in determining the mean corpuscular fragility, two of the most important landmarks in the recognition of variations in the process.

But apart from the above varying accuracy of these two types of estimation of haemolysis, it would appear that perhaps they reveal different stages in a process which is more complicated than is usually assumed. If this is so, then the two methods cannot be expected to give similar results. Much confusion has arisen in this connexion because of the crude idea which prevails regarding the result of the suspension of the red cell in a hypotonic solution of saline. The general conception would seem to be that in a hypotonic saline solution the red cell swells and ruptures with the liberation of its contents. That this is not what happens anyone can observe for himself by watching the effect of a drop of distilled water or hypotonic saline on a drop of blood in a wet preparation under the microscope. The red cells certainly swell but they do not rupture to permit of the escape of the haemoglobin. The haemoglobin would rather seem to diffuse through the intact cell membrane so that the cell becomes

pale and a mere ghost of its former state. Ultimately the cell structure does disintegrate but a proportion of these ghost cells persists and they can still be seen with careful focusing. Hence there are in truth two stages in the process, haemosmosis (escape of haemoglobin) and stromatolysis (disintegration of the cell).

This phenomenon had been noted apparently independently by some previous workers (Spiro, 1897; Rohonyi, 1916; Adair, Barcroft, and Bock, 1921; Brinkman and Szent-Gyorgi, 1924), but its true significance and importance in the estimation of haemolysis have been revealed in an ingenious experiment devised by Ladkin and Macfarlane (1945). By using the sediment of blood which had been lysed by dialysing against distilled water and observing under the microscope the effect of adding sufficient of a concentrated saline solution to bring the mixture up to 1 per cent. NaCl, Ladkin and Macfarlane state that 'a remarkable transformation is seen. Out of the ghost concentrate in which few outlines can be distinguished, there materializes cells which in shape, size and colour are normal red cells. In every case the change is accompanied by a marked decrease in volume.' These workers have also found that as much as 10 per cent. of the haemoglobin can be removed from these ghost cells which are not observable and thus calculable in the ordinary cell-count chamber, so that if a special point is to be made of the accuracy of any particular method, it is the one which depends on estimating the number of unlysed cells rather than the one which notes the amount of haemoglobin diffused into the medium which is the less accurate. On these grounds it might be surmised that the method of counting the cells would tend to overestimate the severity of the process, and this is indeed what is observed from a comparison of the findings of Creed (noting the escape of haemoglobin) and those of Whitby and Hynes (noting the disappearance of red cells).

It is remarkable, however, how few of the workers studying the question of the fragility of the red cell in infancy and childhood, whatever the method employed, have taken into consideration certain extrinsic factors which have long been known to modify the resistance of the cell. Although it has long been known that the CO_2 content of the blood has a definite effect so that venous blood is more fragile than arterial blood, with capillary blood occupying an intermediate position, yet in not one of the above-mentioned investigations was this factor taken into consideration. Some workers used venous blood and others capillary blood so that, others things being equal, it could not be expected that similar results would be obtained. It may be for this reason that the increased fragility in the new-born was reported by some authors because the conclusions were drawn from the examination of cord blood, or from blood obtained by puncture of the longitudinal sinus.

Another factor of considerable importance in assessing the findings is the relative amounts of cells and plasma. The greater the relative amount of the salt-containing plasma to cells, the higher will be the ultimate saline concentration of the mixture. Dacie and Vaughan (1938) have shown that by adding one drop of blood of 20 per cent. packed-cell volume and one drop of blood of 60 per cent. packed-cell volume to 1 c.c. of saline dilution of 0·38 per cent. a difference of 4 per cent. in the final saline concentration results, being 0·398 per cent. with the former and 0·382 per cent. with the latter. For this reason there will seem to be an increased resistance of the red cell in anaemia, and for the same reason it would seem not improbable that some authors may have concluded that the red blood cell in the new-born is less resistant than during adult life because during the neonatal period of life the packed-cell volume is habitually nearer 60 per cent. than the normal adult level of 45 per cent.

Material and method

The subjects of the present investigation were all apparently normal children and were inmates of the Maternity Department and of the Children's Department, The Radcliffe Infirmary, Oxford.

The foetal blood was obtained from the umbilical cord immediately after birth and before pulsation had ceased. From the younger infants blood was obtained from a scalp vein or longitudinal sinus and from the older children from an arm vein. The blood was invariably collected in heparinized containers as this was found to be the only way in which haemolysis could be prevented before treatment with the hypotonic saline. Oxalate was found almost invariably useless for this purpose, particularly in the case of foetal blood, so that any studies of this question in the blood of the foetus and the newly-born in which oxalate has been the anti-coagulant employed are viewed with much scepticism.

As it was believed that it is easier to differentiate between shades of colour than between varying numbers of cells per unit volume, it was decided to investigate the question by noting the rate of diffusion of haemoglobin into the saline diluent. Moreover, as it is particularly easy to differentiate between colours when they are faint, this method would seem to have the distinct advantage of enabling the observer to note the start of the process, as also the 'median corpuscular fragility,' departures of which from the normal are the most constant features of conditions in which the fragility of the red cell is modified. In order to eliminate all possible disturbing extrinsic factors the method of Creed as modified by Dacie and Vaughan (1938) was employed. By this method the blood is collected by venepuncture in heparinized containers and, from the haematocrit reading, the proportion of cells to plasma is brought to the ratio of 45 and 55 respectively. This mixture is thereafter thoroughly oxygenated by exposure to the air. This is attained by gently revolving a thin layer of the blood in a small flask. The dilutions of the saline solution employed were also as recommended by Dacie and Vaughan, differing from each other by 0·02 per cent.

Results

In all, the blood of 98 children has been examined, with the following age distribution:—thirteen during foetal life, twenty-two during the first week of life, fifteen during the second week, eight during the third week, six during the fourth week, eleven during the second month, five during the third month, seven varying between four and six months of age, four from seven to twelve months and seven during childhood.

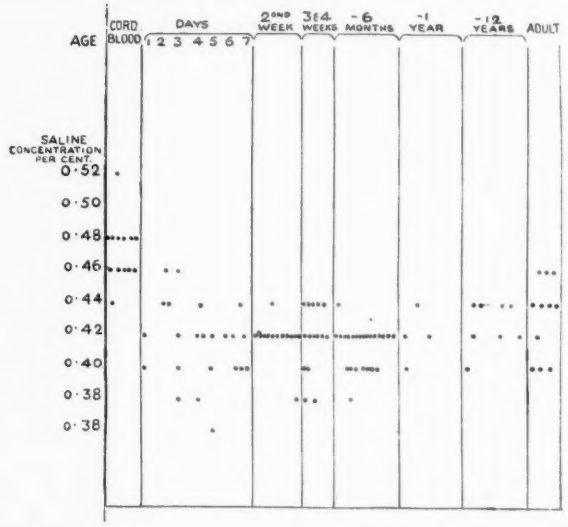

FIG. 1.—Saline concentration at which haemolysis begins according to age.

Details of the findings in these 98 cases are given in the appendix, a general survey of which shows on the whole remarkably little variation. For a better comparison, however, the results are presented in the form of three graphs.

The start of haemolysis. In fig. 1 the saline concentration at which haemolysis begins is plotted according to the age of the child, and from this it is seen that there is a slight but definite difference between the results obtained during foetal life and those obtained during post-natal life. During foetal life haemolysis begins with hypotonic saline dilution varying between 0·52 and 0·44 per cent., but most frequently between 0·48 and 0·46 per cent., whereas after birth haemolysis never starts with dilutions of more than 0·44 per cent., unless during the first two or three days of life. Creed gives the average dilution with which haemolysis begins in the adult as 0·44 per cent., so that it would appear that during foetal life there is a slightly diminished resistance and after birth a slightly increased resistance.

Median corpuscular fragility. In fig. 2 the saline concentration at which 50 per cent. haemolysis occurs is plotted according to age. Here again it is seen that there is a slight but definite difference between foetal blood and blood obtained after birth. In cord blood 50 per cent. haemolysis is found to occur with saline concentrations varying between 0·33 and 0·43 per cent. but chiefly with concentrations of more than 0·35 per cent., whereas after birth 50 per cent. haemolysis is noted to occur with saline concentrations of less than 0·35 per cent. This difference between foetal and post-natal life is well displayed in the following table giving the average concentrations at which 50 per cent.

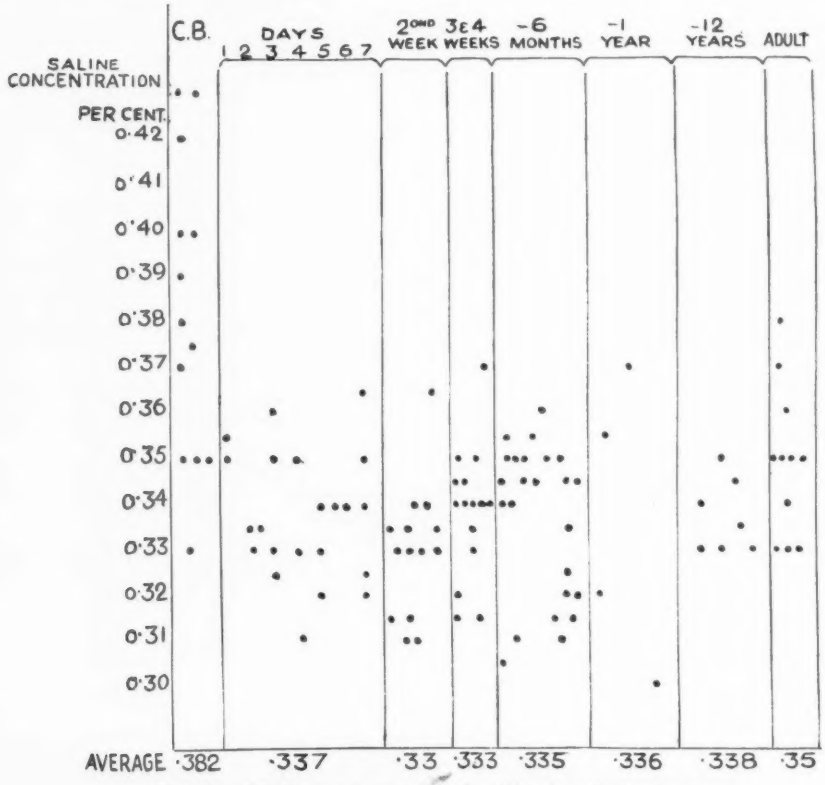

FIG. 2.—Median corpuscular fragility in relation to age.

haemolysis (median corpuscular fragility) was noted at different ages. In this table is given the average

Age ..	Foetus	1/52	2/52	3 and 4/52	–6 mth.	–1 yr.	1 to 12 yr.	Adult
M.C.F.	0·382	0·337	0·33	0·338	0·335	0·336	0·338	0·35

of eleven estimations of mean corpuscular fragility in the case of the adult made during the same period of study. In those eleven adults the mean corpuscular fragility ranged between 0·33 and 0·38. Creed gives the range in the normal adult between 0·342 and 0·387 per cent. saline, so that again there is revealed during childhood a slight increase in resistance of the red cell to hypotonic saline and during foetal life, on the contrary, a slight decrease in resistance.

Complete haemolysis. The determining of complete haemolysis is a matter of no little difficulty

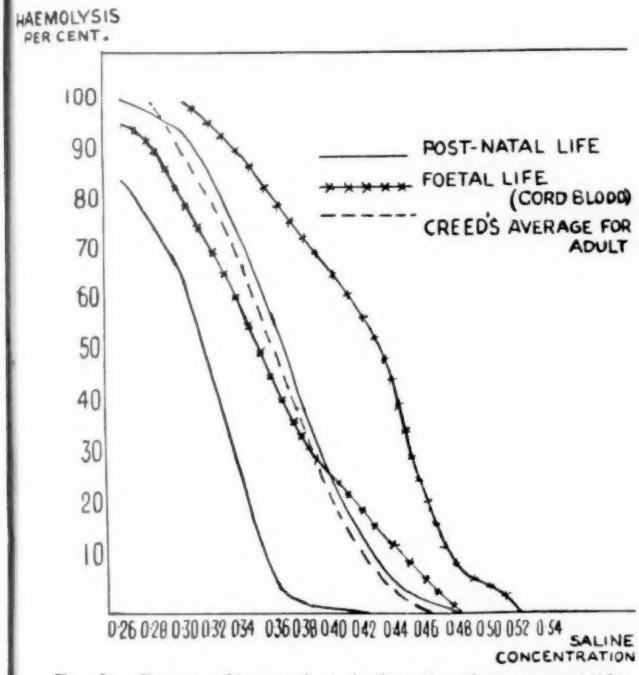

FIG. 3.—Range of haemolysis in foetal and post-natal life.

because the comparison of colours of the depth of shade which prevails at such a concentration of haemoglobin is not easy. Moreover, in view of the work of Ladkin and Macfarlane, it would seem unlikely that 100 per cent. of the haemoglobin ever diffuses into the saline solution as amounts up to 10 per cent. remain adsorbed to the corpuscular membrane. It is, however, useful to view a picture of the complete process, and in fig. 3 there is depicted the complete range of haemolysis at the different saline concentrations as observed in the examples of foetal blood examined, with a similar graph of the observations made during post-natal life and in addition a curve of the average degree of haemolysis with the same saline concentrations as found by Creed in the adult. This chart shows in a striking fashion the differences already mentioned, viz:—the diminished resistance in the foetus and increased resistance during infancy and childhood. The ranges are quite separate in their lower portions referring to the start of haemolysis, but they overlap slightly in that section of the graph representing more complete haemolysis. Creed's curve for the adult occupies an almost medial position.

Conclusions

(1) All methods of estimating the resistance of the red blood cell to hypotonic solutions of saline are both qualitative and quantitative.

(2) The only method permitting of trustworthy comparisons is one in which the CO_2 concentration and the relative proportion of cells and plasma are brought to a uniform level.

(3) Creed's method alone fulfils these conditions.

(4) Using Creed's technique (as modified by Dacie and Vaughan), foetal blood shows a slightly diminished resistance to hypotonic saline and the blood of the infant and child a slightly increased resistance to hypotonic saline.

Thanks are due to Prof. Chassar Moir for permission to study the children under his care and to Dr. R. G. Macfarlane for granting facilities for carrying out the investigation and for much valuable advice.

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APPENDIX—LIST OF CASES EXAMINED

C.B.=cord blood. tr.=trace. ft. tr.=faint trace. v. ft. tr.=very faint trace. O=no haemolysis.

No.	Age	Haematocrit per cent.	Per cent. haemolysis												Median corpuscular fragility
			0·26	0·28	0·30	0·32	0·34	0·36	0·38	0·40	0·42	0·44	0·46	0·48	0·50	
1	C.B.	64		95	80	70	45	35	15	15		7	O			0·33
2	C.B.	53	100	90	80	70	55	45	35	25	15	12	5	O		0·35
3	C.B.	62	90	90	90	80	75	70	65	50	40	30	12	2	O	0·40
4	C.B.	56	100	100	100	85	65	55	45	30	15	10	tr.	O		0·37
5	C.B.	57	100	100	95	95	80	65	55	40	12	5	v. ft. tr.	O		0·39
6	C.B.	67	100	100	100	90	90	75	65	55	45	45	18	7		0·42
7	C.B.	55	100	100	95	85	75	70	55	50	42	35	15	6		0·40
8	C.B.	59	98	90	80	65	55	45	35	25	15	10	4	O		0·35
9	C.B.	60	95	90	90	80	70	65	50	40	26	22	6	v. ft. tr.		0·38
10	C.B.	59	100	100	100	95	92	85	75	62	55	45	20	5		0·43
11	C.B.	58	95	90	80	70	60	55	45	35	15	12	3	v. ft. tr.		0·375
12	C.B.	57	100	95	95	95	85	78	70	65	58	45	15	8	5 v. ft.tr.	0·43
13	C.B.	68	100	88	80	68	55	40	18	18	7	7	ft. tr.	O		0·35
14	4 hr.	65	100	100	100	90	80	45	35	15	5	O				0·35
15	14 hr.	62	100	100	90	80	60	40	25	15	5	O				0·35
16	30 hr.	70					80	20	25			10	O			0·33
17	41 hr.	64	95	95	80	70	45	30	15	10	5	ft. tr.	ft. tr.	O		0·335
18	41 hr.	74	100	85	70	60	45	20		20	tr.	tr.	O			0·335
19	2 D. 7 hr.	70		95	80	70	60	45	5	tr.	O					0·35
20	2 D. 9 hr.	60	100	90	85	75	65	55	25	5	5	ft. tr.	v. ft. tr.	v. ft. tr.		0·36
21	2 D. 11 hr.	55	100	95	75	60	35	15	tr.	O						0·33
22	2 D. 16 hr.	58	95	80	70	55	50	20	10	8	5	O				0·325
23	3 D.	62	95	85	75	55	45	25	15	v. ft. tr.	v. ft. tr.	O				0·33
24	3 D. 1 hr.	60		95	80	70	60	35	5	O						0·35
25	3 D. 1½ hr	51	100	100	65	45	30	12		tr.	tr.	O				0·31
26	4 D. 6 hr.	62	95	80	65	55		15	O							0·32
27	4 D. 12 hr.	62		85	80	70	30	25	8	4	O					0·33
28	4 D. 20 hr.	54	95	85	75	65	50	25	15	12	tr.	O				0·34
29	5 D. 14 hr.	54	100	100	90	80		25		tr.	tr.	O				0·34
30	5 D. 18 hr.	64	95		75	60	50	25	10	ft. tr.	ft. tr.	O				0·34
31	6 D.	56	100		70	45		25	7	tr.	O					0·32
32	6 D. 2 hr.	62			95	90	70	60	40	15						0·35
33	6 D. ½ hhr	57	95	90	75	65	55	25	15	tr.						0·34
34	6 D. 13 hr.	65	100	100	95	75		70	45	25		O				0·365
35	6 D. 14 hr.	43		90	70	60	35	20	12	5	tr.	ft. tr.	O			0·325
36	7 D. ½ hr.	61	90	85	80	55	45	25		5	tr.	O				0·335
37	8 D. 1 hr.	67		90	65	35	35	25	15	5	tr.	O				0·315
38	8 D. 1 hr.	55	95	90	80	60	45	15	5	ft. tr.	ft. tr.	O				0·33
39	9 D. 2 hr	52	85	65	55	45	35	15	10	tr.	ft. tr.	O				0·31
40	9 D. 3 hr.	56	95	80	70	55	45	20		tr.	ft. tr.	O				0·33
41	9 D. 3 hr.	58	85	70	55	45	25	5	ft. tr.	ft. tr.	ft. tr.	O				0·31
42	9 D. 12 hr.	52	100	95	85	70	45	15	6	3	v. ft. tr.	v. ft. tr.	O			0·335
43	9 D. 20 hr.	54	95	90	75	45	35	15	12	ft. tr.	v. ft. tr.	O				0·315
44	10 D. 1 hr.	59	100	90	70	70		40	35	10	10	O				0·34
45	11 D. 17 hr.	52	95	85	75	55	45	15	12	ft. tr.	ft. tr.	O				0·33
46	12 ½ D.	59	100	85	85	60	50	40	15	O						0·34
47	13 D. 6 hr.	61	100	100	90	90	75	55	35	15	5	O				0·365
48	13 D. 19 hr.	62	90	85	75	60	45	15	10	5	3	O				0·335
49	13 D. 22 hr.	53	100	90	85	60	45	15	5	tr.	ft. tr.	O				0·33
50	14 D.	56	100	95	80	70	50	15	8	5	tr.	O				0·34
51	14 D.	64	95	90	85	75	50	25	15	12	8	ft. tr.	O			0·34
52	14½ D.	43	85	75	65	45	25	5	v. ft. tr.	v. ft. tr.	O					0·315
53	15½ D.	55	90	90	80	70	55	10	3	O						0·345
54	16¾ D.	55	100	95	85	75	55	25	15	ft. tr.	O					0·345
55	18½ D.	59	95	75	60	50	38	25	18	5	tr.	tr.	O			0·32
56	19 D.	51	100	90	85	75	65	25	15	5	tr.	v. ft. tr.	O			0·35
57	19½ D.	61	95	85	75	65	50	25	10	5	v. ft. tr.	O				0·34
58	21 D.	38	100	90	75	60	30	15	5	O						0·33
59	21 D.	49	95	85	65	55	40	10	5	v. ft. tr.	v. ft. tr.	O				0·315
60	22 D.	50	100	95	75	65	50	25		5	ft. tr.	O				0·335
61	23 D.	48	100	95	90	85	70	30	5	tr.	ft. tr.	O				0·35
62	24 D.	56	100	85	75	60	50	10	5	v. ft. tr.	v. ft. tr.	O				0·34
63	25 D.	44	100	100	80	75	75	25		20	ft. tr.	ft. tr.	O			0·34
64	26 D.	50	100	100	100	90	60	55	50	25	10	tr.	O			0·37
65	31 D.	43	100	90	85	75	55	15	5	v. ft. tr.	v. ft. tr.	O				0·345
66	33 D.	46	90	75	55	40	15	5	v. ft. tr.	v. ft. tr.	v. ft. tr.	O				0·305
67	5/52	33	100	90	75	65	50	5	ft. tr.	v. ft. tr.	v. ft. tr.	O				0·34
68	5/52	35	100	90	75	65	55	35	15	5	ft. tr.	O				0·35
69	5/52	42	100	100	100	90	70	35	25	tr.	ft. tr.	O				0·35
70	6/52	40	100	100	90	80	60	50	8	5	tr.	O				0·355
71	6/52	26	100	90	85	75	50	25	ft. tr.	ft. tr.	ft. tr.	O				0·34
72	6/52	33	90	70	55	45	30	ft. tr.	ft. tr.	O						0·31
73	6/52	34	95	90	85	75	65	30	15	ft. tr.	ft. tr.	O				0·35
74	7/52	28	100	90	85	80	60	25	15	5	ft. tr.	ft. tr.	O			0·345
75	7·52	27	100	95	90	75	55	25	8	tr.	v. ft. tr.	O				0·345
76	8/52	32	100	100	95	85	65	45	25	5	O					0·36
77	8/52	35	100	100	95	80	70	15	tr.	tr.	O					0·35
78	9/52	30	100	90	70	45	25	10	tr.	ft. tr.	O					0·315
79	9/52	33	100	90	85	75	60	25	8		3	O				0·35
80	10/52	25		90	60	35	30	15	5	2	tr.	O				0·31
81	12/5	38	100	95	80	40	40	8	tr.	tr.	O					0·32
82	13/52	37	100	100	90	80	35	10	tr.	tr.	O					0·325
83	13/52	31	85	75	60	50	35	15	10	tr.	O					0·32
84	16/52	38	100	95	85	70	60	35	25	5	ft. tr.	O				0·345
85	17/52	43	95	90	80	65	55	5	ft. tr.	v. ft. tr.	v. ft. tr.	O				0·345
86	5/12	44	94	80	50	65	15	tr.	tr.	ft. tr.	O					0·315
87	5/12	37	100	100	85	65	45	25	15	tr.	v. ft. tr.	O				0·335
88	7/12	35	100	90	70	50	15	5	tr.	ft. tr.	ft. tr.	O				0·32
89	8/12	38	100	100	90	85	65	45	25	5	O					0·355
90	11/12	31	100	100	100	90	80	65	35	25	15	3	O			0·37
91	3 yr.	36		90		70		15		5	O					0·33
92	3½ yr.	36		90	90	80	30	15	tr.	tr.	ft. tr.	ft. tr.	O			0·33
93	3½ yr.	33			70		45		8		2	O				0·33
94	8 yr.	37	100	100	100	90	80	35	25	tr.	ft. tr.	O				0·35
95	10 yr.	40	100	100	90	85	55		10	ft. tr.		ft. tr.	O			0·345
96	11 yr.	41	100	100	90	80	50	35	12	5	tr.	tr.	O			0·34
97	13 yr.	24	100	95	85	65	35	5	ft. tr.	ft. tr.	v. ft. tr.	v. ft. tr.	O			0·33

TOXIC THROMBOCYTOPENIC PURPURA FOLLOWING LOCAL SULPHATHIAZOLE THERAPY

BY

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In spite of the universal use of sulphonamides there have apparently been reports of the occurrence of purpura following their administration on only twenty-two occasions. In fourteen cases the thrombocytes were found to be reduced in number, absent from blood films or below 100,000 per c.mm.; in four cases the thrombocyte count exceeded 125,000 per c.mm. and in four the count was not recorded. In all cases the drug was given by mouth and the amount producing purpura varied between 4 and 45 gm. In six cases purpura followed interrupted administration, the interval varying between one day and three years. The literature on the subject has recently been referred to more fully by Sherlock and White (1944). The case here reported is of interest in that thrombocytopenic purpura followed the local application of a 5 per cent. sulphathiazole ointment, and for the light which the investigations throw upon the mechanism of the condition.

Case history

A. M., a boy, aged twelve years, was admitted to hospital on October 27, 1943. Four days previously a few small areas of impetigo were noticed on the face and on the right foot. An ointment containing 5 per cent. sulphathiazole was applied to these areas twice daily for two days. On the evening of the second day his nose began to bleed and a purpuric rash appeared on his body. He was admitted to hospital the following morning. He had previously been a healthy child and there was nothing of note in his personal or family medical history. There was no evidence of allergic manifestations or of any haemorrhagic diathesis in himself or in any of his relatives. He had never had sulphonamide drugs before.

On examination he was a sturdy well-nourished child. The temperature was 98·6° F. There was profuse bleeding from both nostrils. The lips, around which the sulphathiazole ointment had been applied, were swollen and blood was oozing from them freely. There was no bleeding from the gums and no visible submucous purpura in the mouth. The whole of his body, including the face and limbs, was covered with a purpuric rash, the haemorrhagic areas varying between 1 mm. and 1 cm. in size. There were no large ecchymoses and no retinal haemorrhages. There was no blood in the urine but occult blood was present in the stool. The liver and spleen were not clinically enlarged, but enlarged glands in the axillae and neck were palpable without tenderness. Three small areas of impetigo, each approximately the size of a sixpenny-piece, were noted on the face and right leg.

EXAMINATION OF THE BLOOD immediately on admission to hospital gave the following results:—R.B.C. 4·12 million per c.mm.; Hb. 11·0 gm. per 100 c.mm. (Haldane); C.I. 0·97; reticulocytes 1 per cent.; W.B.C. 10,800 per c.mm.; polymorphonuclear neutrophils 75 per cent., eosinophils 4·5 per cent.; basophils 1 per cent.; lymphocytes 12 per cent.; monocytes 6 per cent.; Türck cells 1·5 per cent. Subsequent examinations during treatment showed no significant reduction in the number of granular cells. Thrombocytes (direct method 3·8 per cent. citrate diluent) 20,000 c.mm. Bleeding time (Duke) over 30 minutes.

On October 29, 1943, the coagulation time (Lee and White) was 11 minutes and the clot retraction (Macfarlane) 18 per cent. at 1 hour.

Capillary resistance. Positive pressure, tourniquet (Hess) test positive; negative pressure (Scarborough) 100; 100; 100. These figures represent mm. Hg suction required to produce a single petechia in each of three ' standard ' areas of skin on the front of the forearm. They indicate a low capillary resistance.

Sternal puncture showed a reactive normoblastic bone marrow with excessive eosinophils and megakaryocytes. Thrombocytes were absent from all the marrow smears examined.

Repeated observations were made on the bleeding time (Duke method from the ear), thrombocyte count (direct method with 3·8 per cent. citrate diluent) and capillary resistance [negative pressure method of Scarborough (1941a)]. The results are plotted in the chart (fig. 1), the values for capillary resistance being given separately for each of the three ' standard ' areas.

PROGRESS AND TREATMENT. Epistaxis was temporarily controlled by packing the nose with gauze saturated with snake venom (' Stypven ') and a transfusion of 1 pint of fresh blood given immediately into a vein. The next day there was gross haematuria, fresh epistaxis and further petechial haemorrhage and bleeding from the lips. The snake venom pack was renewed and a further pint of fresh blood transfused. Following this transfusion the temperature rose to 102·8° F. During the next four days the patient was transfused daily with half a pint of fresh blood and the nose was repacked at

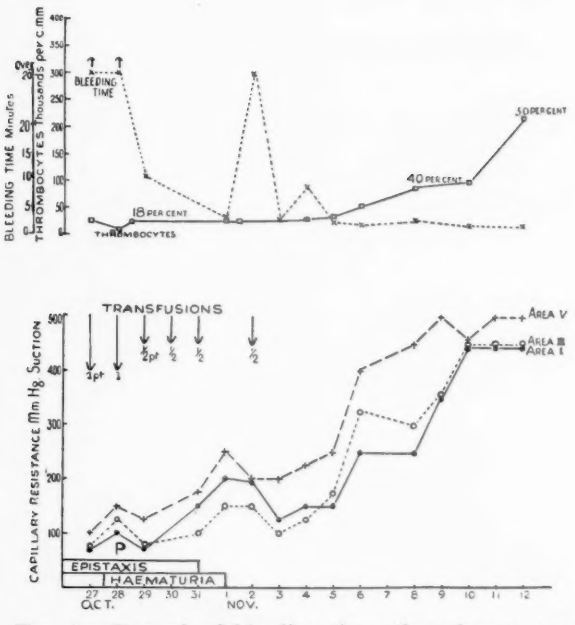

FIG. 1.—Record of bleeding time, thrombocyte count and capillary resistance (left arm) in A.M. with secondary thrombocytopenic purpura. P=purpura. Figures alongside record of thrombocyte count are values for clot retraction (Macfarlane's method).

intervals with gauze saturated with snake venom. Recovery was rapid after the fifth transfusion and no further treatment was required.

Discussion

The relationship between bleeding time, thrombocyte count, capillary resistance and the haemorrhagic manifestations is shown in fig. 1. During recovery from the bleeding phase, possibly as the result of repeated transfusion, the bleeding time fell and the capillary resistance increased, the thrombocyte count remaining below 50,000 per c.mm. On November 1, when bleeding ceased, the capillary resistance was double its initial values in all three standard areas and the bleeding time was 3 minutes. The platelets, however, were still under 50,000 per c.mm. The association of a normal bleeding time with a thrombocyte count below 50,000 per c.mm. is well known to occur in the course of thrombocytopenic purpura. Previous experience, confirmed in this case, indicates that this may be due to an increase in capillary resistance above the level which, in association with thrombocytopenia is responsible for the development of bleeding and suggests that the level of capillary resistance is a critical factor in the production of purpura and in determining the length of the bleeding time in this disease. During the non-bleeding phase of recovery (November 1–10) both bleeding time and capillary resistance had achieved satisfactory levels before the thrombocyte count reached 100,000 per c.mm. Thereafter the capillary resistance was maintained at a high level and the bleeding time below 5 minutes whilst the platelets gradually increased to 400,000 per c.mm. It has previously been reported (Scarborough, 1941b) in subjects normal in respect of bleeding time, coagulation time and thrombocyte count, that the extravascular suffusion of blood into the tissues, or into the alimentary canal is capable of producing a marked and immediate increase in capillary resistance. A similar result follows the intramuscular injection of blood and is also found within 6 hours after blood transfusion (Scarborough, 1941a). This phenomenon, which is striking, may also be observed in certain of the bleeding diseases, for example, in scurvy, haemophilia and hypoprothrombinaemia. In the present case the presence of the patient's blood under the skin and in the renal and alimentary tracts was not associated with an immediate increase in capillary resistance nor was this observed after any or all of the six blood transfusions, although, however, a gradual increase in capillary resistance in all three standard areas occurred during this period. It is suggested, therefore, that in this respect the behaviour of the capillaries in the bleeding phase was unusual. These observations tend to emphasize the importance of the vascular factor in the production of bleeding in thrombocytopenic purpura. In this connexion it is interesting to recall the observations of Macfarlane (1941) who was able to demonstrate by direct capillary microscopy in cases of thrombocytopenic purpura a defective capillary contractility.

The striking features of this case following the local application of sulphathiazole to the broken skin suggested that an attempt be made to investigate the effects, particularly on the capillaries, of the application of sulphathiazole to the intact skin under controlled conditions. Accordingly a 'test area' was marked out on the centre of the volar aspect of both forearms. On November 15 a piece of gauze 1 inch square covered with a layer of 5 per cent. sulphathiazole in eucerin was applied under strapping to an area of skin in the middle of the anterior surface of the right forearm for 1½ hours. Immediately following this application a significant reduction in capillary resistance was found in two out of three standard areas (one at the elbow and the other at the wrist) on the opposite (left) arm—A in fig. 2. The application of a similar patch for 1½ hours to the corresponding 'test area' on the left forearm on November 17 was immediately followed by a highly significant fall in capillary resistance in all three standard areas on the same (left) forearm—B in fig. 2—and a significant fall in capillary resistance in all three standard areas on the opposite (right) arm. By the next morning (18 to 20 hours later), on both occasions and in all areas, the capillary resistance had returned to the high level found before the test was made. Observation on the thrombocyte counts before and after these applications of sulphathiazole showed on the first occasion a fall of 95,000 per c.mm. and on the second a fall of 105,000 per c.mm., co-incident with the reduction in capillary resistance. It is possible that these differences may be significant also. On November 26 a 'patch test' of 5 per cent. sulphanilamide in eucerin was applied for 1½ hours to

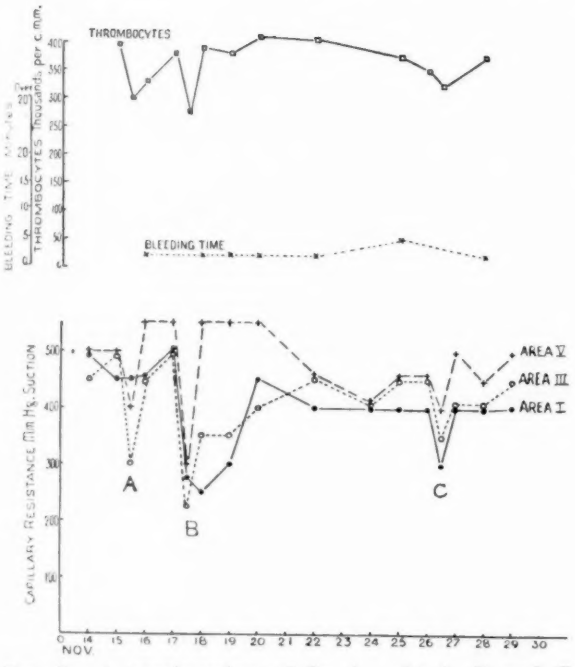

FIG. 2.—A continuation of fig. 1. At A, B and C. sulphonamide was applied to the unbroken skin. For further explanation see text.

the test area on the left arm. Six hours after its removal the capillary resistance was again found to be significantly reduced in all areas in both arms (C in fig. 2) but no significant alteration in platelet count was detected. Twenty-four hours later the capillary resistance had risen to the high level observed before the test.

Further evidence that the local application of sulphonamide drugs to the intact skin of the patient could produce a fall in capillary resistance was obtained by determinations of capillary resistance in the ' test areas ' both before and after the application of the patch tests. The results with sulphathiazole and sulphanilamide are given in table 1. In each case the application produced a marked fall in capillary resistance in the test area and also, though to a smaller extent, in the corresponding area on the other arm. A control test with eucerin alone produced no measurable effect. Similar experiments with three other subjects, two of whom had received sulphapyridine previously and one of whom (J. D.) had a level of capillary resistance considerably lower than the patient A. M. at the time he was tested all gave negative results even after the application of sulphonamide for 13 to 24 hours.

These experiments show that sulphonamides can be absorbed through the intact skin from a eucerin base in sufficient amount to produce effects upon the capillary walls of a ' sensitive ' subject both at the site of application and in parts remote from it. It is not considered that unequivocal evidence of a reduction in thrombocyte count following the application has been obtained. Since there is no reason to suppose that the absorptive properties of the skin of the patient were in any way unusual, it is suggested that observations on capillary resistance after the application of similar patch tests, or even after oral administration might afford a means for detecting sulphonamide sensitivity. In this connexion it is interesting to recall the observations of Park (1943) who, writing of cutaneous hypersensitivity to sulphonamides, came to the conclusion that ' intradermal and patch tests were of little value in diagnosis.' Hurd and Jacox (1943) were also unable to demonstrate skin sensitivity in one of their cases which, however, was shown to be sensitive to sulphonamide by mouth. If these investigations are considered on a quantitative basis it is clear that the amount of sulphathiazole applied to the intact skin required during the experimental period to produce a fall in capillary resistance in A. M. was small—of the order of 0·05 gm. Furthermore the total amount of sulphathiazole applied to the broken skin which originally caused throm-

TABLE I

OBSERVATIONS ON CAPILLARY RESISTANCE IN ' TEST ' AREAS BEFORE AND AFTER PATCH TEST OF SULPHONAMIDE DRUGS

Subject	Date	Test Material	Time applied Hours	' Test ' arm	Capillary resistance in ' test ' areas			
					' Test ' arm		Opposite arm	
					Before	After	Before	After
Patient A.M.	17 Nov.	Sulphathiazole	1½	Left	500	200	300	200
Aged 12	26 Nov.	Sulphanilamide	1½	Left	500	250	400	250
	28 Nov.	Eucerin	1½	Left	400	450	300	350
Control J.N.	31 Jan.	Sulphapyridine	1½	Right	400	350	500	500
Aged 37	1 Feb.	Sulphapyridine	18	Left	500	500	350	350
Control W.M.	28 Jan.	Sulphanilamide	1½	Right	350	450	450	450
Aged 28	29 Jan.	Sulphathiazole	13	Left	450	350	300	300
Control J.D.	28 Jan.	Sulphathiazole	1½	Right	250	350	300	300
Aged 15	30 Jan.	Sulphathiazole	13	Left	300	300	200	250
	8 Feb.	Sulphapyridine	18	Right	250	250	250	250
	9 Feb.	Sulphanilamide	24	Left	300	300	250	200

bocytopenic purpura can hardly have exceeded one gramme. It was, therefore, considered unjustifiable to administer test doses of sulphonamide by mouth to this case. In the case of Hurd and Jacox (1943) thrombocytopenia originally occurred after the oral administration of 14 gm. of sulphathiazole in the treatment of pneumonia. After recovery small doses of both sulphathiazole and sulphadiazine (3 doses of 1·5 gm. of each) given by mouth were followed by an increase in bleeding time with a marked fall in thrombocyte count and a positive tourniquet test. Rosenfeld and Feldman (1942), however, gave a second course of sulphathiazole to a patient with renal calculus who initially developed thrombocytopenia after the administration of 5·5 gm. of sulphathiazole. No further purpura occurred. It would appear possible, therefore, that this type of sulphonamide sensitivity may be a temporary phenomenon.

The patient here described proved to be sensitive to the local application to the intact skin of both sulphathiazole and sulphanilamide and the patient of Hurd and Jacox was sensitive to both sulphathiazole and sulphadiazine administered by mouth. This serves to underline the already well-known fact that sensitivity is towards the sulphonamide group of drugs rather than towards any individual member of the group.

When taken together with the fatal case of purpura of the vascular type following sulphapyridine therapy reported by Sherlock and White (1944) in which the 'capillary resistance by a positive pressure method indicated very marked fragility' and in which 'the platelet count, although low (120,000) had not been reduced to the level usually associated with bleeding in essential thrombocytopenic purpura,' these observations on the effect of sulphonamides on capillary resistance strongly suggest that it is the vascular factor which is of primary importance in the production of secondary thrombocytopenic purpura.

Summary

A case of symptomatic thrombocytopenic purpura in a boy, aged twelve years, is described following the local application of 5 per cent. sulphathiazole ointment for impetigo.

After return of the platelet count and capillary resistance to normal levels the application of sulphonamides to the intact skin produced striking reductions in capillary resistance at, and away from, the site of application. Less striking falls in platelet count were noted.

It is considered that these observations point to the importance of the vascular factor (low capillary resistance) as the basis of toxic thrombocytopenic purpura.

Thanks are due to Professor L. S. P. Davidson for permission to study the case and for his continued interest and advice throughout the investigation.

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THE DIAGNOSIS OF CHRONIC INTUSSUSCEPTION IN CHILDREN

WITH AN ACCOUNT OF THREE CASES

BY

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Chronic intussusception in children is uncommon. As a clinical entity it is not well known. Still (1921) gives the clearest account:

'On a particular day the child seemed to have pain in the abdomen and vomited once or twice. During the next few days he occasionally vomited, generally in association with a colicky pain. The vomiting has become less frequent, only once in two or three days, and the pain is only occasional. The bowels, which before were open daily, have since the onset been less regular, aperients have been necessary, but when given have worked well and the stools have been normal; there has been no blood in the stool or at most there has only been a streak once or twice, such as might be seen on the stool of any constipated child. The symptom which has troubled the parents most is the wasting; the child after three or four weeks of these vague troubles is obviously getting thin. The temperature throughout has been normal. Such is the history, and with a duration of some weeks even the finding of a more or less definite lump in the abdomen may hardly raise a suspicion of intussusception, especially when the mother's chief complaint is the wasting. Nevertheless, it is by the detection of the more or less sausage-shaped tumour, and especially by its varying consistency from moment to moment during palpation, that the diagnosis is to be made; to the tactus eruditus also the unnatural emptiness of the right iliac fossa (Dance's sign) may be useful confirmatory evidence, as in the ordinary acute intussusception.'

The purpose of this paper is to describe three cases, which, though conforming to Still's description in some respects, were not diagnosed for a long time, owing to the apparent absence of an abdominal tumour in two of the cases. Previous case reports are given in an appendix.

Case records

CASE 1324. (43). A boy aged seven-and-a-half years was referred to the Radcliffe Infirmary by Dr. W. Stobie on November 12, 1942.

When two-and-a-half years old he was admitted to a hospital in Chester with a sudden attack of severe abdominal pain. No operation was performed and he recovered within two days. In March, 1939, he was admitted to the private ward of the Radcliffe Infirmary with a purpuric rash and pain and swelling of various joints. Some days previously he had complained of abdominal pain. His bowels were constipated, but there was never any blood in his stools and nothing abnormal was felt in his abdomen. The diagnosis was a purpura of the Henoch-Schönlein type, but its exact etiology was not determined.

After his discharge from hospital he was kept under periodic observation. His general health remained good but he continued to have attacks of abdominal pain. Each attack seemed to follow increasing constipation. It was not accompanied by fever, bruising or purpura, but he was said to look very pale. The pain was of a colicky nature and it usually passed off in the night. These attacks recurred about once a month.

The last attack started five days ago and was characterized by severe abdominal pain, which caused him to scream. The pain was centred around the umbilicus and occurred in spasms about every hour. It was severe for two days and then seemed to subside, but it returned about twelve hours before admission, and his bowels were moved for the first time since the onset of the pain. The motions were normal.

On examination, he was an alert, intelligent and co-operative boy. He looked healthy, but at times was troubled with bouts of pain. His pulse and respirations were normal. There was some resistance in the abdomen to the left and slightly below the umbilicus, which seemed to be due to hardening of the left rectus. The signs were unaltered during the paroxysms of pain. The next day he was much better and in the following ten days he had only one or two spasms of pain. On account of his previous history, various haematological investigations were carried out, but all revealed normal findings. Dr. V. Walker made certain skin tests but no food allergy was detected. A barium meal was advised and this was given on January 19, 1943. The stomach and duodenum were normal, but the follow-through (fig. 1) revealed an intussusception with its apex reaching just beyond the hepatic flexure of the transverse colon. No attempt was made to reduce it. At operation (Mr. D. C. Corry) the intussusception was reduced by manipulation. There were no adhesions, but the gut was swollen and slightly reddened. Appendicectomy was performed and one large mesenteric gland was removed, the histological examination of which did not show any specific lesion.

FIG. 1.

Convalescence was uneventful until February 10, when he was re-admitted with severe intestinal colic of seven hours duration. Laparotomy revealed a loop of small bowel bound down by adhesions. The adhesions were divided and he made a good recovery. Seven months later, his mother reported that he was quite well.

Comment. It is not known for certain how long this boy had had an intussusception, but his history suggests that it first happened when he was two-and-a-half years old, i.e. five years ago. On this occasion, spontaneous reduction must have occurred, for he remained free from symptoms for about two years. Three years ago he had an illness which was in the nature of a toxic reaction of the Henoch-Schönlein type, and there can be little doubt that the intussusception was caused at this time, for thereafter he had attacks of pain about once a month. Despite the long standing illness, the boy's condition remained good and there was no wasting. The true diagnosis was never suspected because no abdominal tumour was palpated even during the paroxysms of pain. The radiological examination gave conclusive evidence of intussusception.

CASE 8340. (43.) R. S., a boy aged eight years, four months, was admitted on April 25, 1943, with the following history:

On March 31, on returning home from school, he collapsed on the sofa. During that night he complained of pain in the lower abdomen, vomited undigested food and passed a loose motion in which there were streaks of blood. The following day his family doctor made a diagnosis of gastro-enteritis. He was kept in bed for three days on a milk diet, and then as he seemed better, he was allowed to get up. The same evening he had another attack, which was similar to the first, but more severe. On this occasion he was sent to the Victoria Hospital at Swindon. Here, it was found that the right side of the abdomen was tender and that there was some muscular guarding. The pulse and temperature were normal. Among the conditions which were considered were intussusception, tuberculous enteritis and acute appendicitis. At first he was constipated, but on the third and fourth days his bowels opened naturally, abnormally large stools being passed. The tenderness disappeared and the Mantoux tuberculin test proved negative. A consulting physician suggested that as he seemed quite well, he was discharged from hospital (April 18).

On the evening of his return home, he had another attack. Three days later he had yet another, and on this occasion he complained of much pain and six hours later passed about five ounces of blood. Two days later he was admitted to the Radcliffe Infirmary. He was now so pale that his doctor sent him for a blood transfusion.

His mother stated that before the illness began the boy had been a ravenous eater, but recently his appetite had been very poor. She thought that he had lost a lot of weight. He had never been a robust child, but had had no other severe illnesses. His mother's eldest brother died from tuberculous peritonitis, but there was no other case of tuberculosis in the family.

On examination he was a spare, rather sallow boy with a slight malar flush. His rectal temperature was 100° F. There was some slight resistance to palpation, particularly on the right side of the abdomen, but no apparent tenderness. The liver and spleen were not palpable. The rectum was full of soft, normal coloured faeces and there was no blood on the examining finger.

During the first ten days he lay listlessly in bed, sometimes complaining of pain in the left hypochondrium. His appetite was poor and he vomited five times. On May 7 he was seen by Prof. L. Findlay, who noted that the abdomen was full, especially in the left epigastrium and hypochondrium. He detected an indefinite mass running from the left hypochondrium to slightly above the midline just above the umbilicus; it could just be felt on rectal examination. Irritation of the abdominal wall induced peristaltic waves running from left to right along the line of the mass, apparently in the stomach.

Three days later, careful palpation of the abdomen revealed that the lower border of the mass extended from below the costal margin to beyond the midline, just above the umbilicus, and it could be seen bulging the abdominal wall. The upper border was less well defined. The mass was not attached to the abdominal wall and it moved with respiration. It was dull to percussion and continuous with splenic dullness. Later the same day, the tumour changed its position slightly and one of us thought that it could be felt to grow harder and softer. Two days later there was little change.

The diagnosis was not clearly determined. The question of intussusception was considered, but because of the position of the tumour and the route of the peristalsis, it seemed that there might be a tumour affecting the stomach and, for this reason, a

FIG. 2.

barium meal was requested. This was carried out on May 13. The stomach and duodenum were normal, but a follow-through (fig. 2) revealed an intussusception of the ileo-colic variety, with its apex just beyond the splenic flexure. It was decided to attempt to reduce it with a barium enema under observation with the fluorescent screen. The enema forced the apex of the intussusception backwards into the ascending colon, but the intussusception could not be completely reduced. The boy experienced only slight discomfort from this procedure and until his operation remained quite well.

On May 20 the child was operated upon and found to have an ileo-caecal intussusception. It could not be reduced by manipulation, and the base of the caecum and the appendix had to be excised. No cause was seen. The child made an uneventful recovery, and six weeks later he was quite well.

Comment. On looking back it will be seen that the history was typical. It began with a sudden attack, characterized by collapse, abdominal pain, vomiting and the passage of blood-stained faeces, from which he recovered within three days. Later, there were many other similar attacks and on one occasion he passed a considerable quantity of blood per rectum. The child's appetite failed and he lost a lot of weight. At first no abdominal tumour was recognized and for a long time the diagnosis of intussusception was never seriously entertained. Later, careful palpation disclosed a tumour, but even then the diagnosis was not obvious, for in some respects its physical characters were misleading. On the contrary, the radiological findings gave conclusive evidence of the true nature of the complaint.

CASE 3. A.G., a boy aged seven years, was admitted to the Radcliffe Infirmary under the care of Dr. A. Cooke on August 31, 1944. He had been perfectly well until two months ago, when after eating gooseberries he complained of a pain in his stomach. The pain came on quite suddenly, but only lasted a minute or two and then passed off. Next day, he was off his food and vomited everything he took by mouth, but he had no further pain. His doctor saw him three days later. He was emaciated and had a tumour running across the epigastrium, downwards and obliquely from left to right. The following day, the sickness had ceased and the tumour had disappeared. He was allowed to resume solid food the next day and on the following day his sickness began again, his temperature rose and the tumour reappeared. He was admitted to a hospital and a week later was discharged. Two days later, the abdominal pain recurred. It came on every two minutes and lasted a second or two. The child described the pain as ' not like a stomach ache but like something pricking him.' He was re-admitted to a hospital and a barium meal and enema were performed which were reported to reveal no evidence of obstruction.

He was in hospital about six weeks and throughout this time he seemed to be getting worse. Fluids were taken and he appeared to improve on them, but if he was given solid food his temperature rose to 102° F. and he began to vomit. Accordingly, his doctor decided to refer the child to the Radcliffe Infirmary for further investigation.

On admission he was found to be undersized and mentally retarded. He had marked generalized muscular wasting, an odd-shaped skull and a curious cardiac murmur suggestive of congenital disease. The abdomen was protruberant but not tender, and no mass was felt. A barium enema was carried out on September 14, 1944, by Dr. B. Mannheimer and this revealed a filling defect in the ascending colon—the appearances being typical of intussusception. There were large amounts of occult blood in the stools. His haemoglobin level was 60 per cent. For several days special efforts were made to improve his general condition. On September 18, he was reported to have vomited his food, but on examination one hour later, no abdominal tumour could be felt. He said he had pain and pointed to the region of his umbilicus. Operation was performed September 23. Preliminary transfusion was unnecessary as his haemoglobin had risen to 76 per cent. The operation (Mr. D. C. Corry) disclosed an intussusception of the ileo-caecal variety reaching as high as the ascending colon. Reduction by manipulation was attempted but several areas of necrosis were revealed so the affected bowel was resected. Examination of the specimen revealed no predisposing causal factor. The child made a satisfactory recovery and was ultimately discharged without complaint, but he was still very emaciated.

Comment. It is probable that this boy had had an intussusception for about three months. At the beginning the story was characteristic and a lump was palpable, but within twenty-four hours of the child being brought under observation, the symptoms

FIG. 3.

subsided and the lump disappeared. The subsequent history is more confusing. The boy suffered from repeated attacks of vomiting accompanied by a rise in temperature. He had some pain but it was never severe. No lump was palpated. The doctor submitted the boy for a gastro-intestinal investigation, but gained little help for the barium meal and enema were reported to show no signs of obstruction (it is not known whether the examinations were performed by an experienced radiologist). Since the child made no sustained improvement in health, he was referred to the Radcliffe Infirmary for a further opinion. A second radiological examination (fig. 3) showed the intussusception quite clearly, but though the child was kept under observation for three weeks, no lump was ever detected by ordinary clinical examination. The history was very difficult to analyse on account of the child's mental state, but there is no doubt that he did have some recurrent attacks of central abdominal pain, though except on the first occasion, the pain was never very severe.

No difficulty was experienced in making a correct radiological diagnosis for the intussusception was visualized. (With regard to the findings of the first examination it should be noted that chronic intussusception does not cause intestinal obstruction.)

Discussion

Judging from the reports in the literature, the diagnosis of chronic intussusception in children is seldom easy. Generally, some weeks or months elapse before the true nature of the condition is realized, and sometimes it is never suspected until revealed by operation or at autopsy. It seems that mistakes arise because the whole clinical picture is not given careful consideration. The significance of repeated attacks of abdominal cramp is not appreciated and too little attention is paid to the physical examination.

Since Still wrote his paper many of the standard textbooks have emphasized the presence of a tumour; for instance: 'A child may have attacks of abdominal pain at hourly intervals for some weeks and on examination a mass is to be found' (Paterson). Again 'only the presence of a tumour leads to recognition of the condition' (Holt and McIntosh). 'The correct diagnosis is arrived at by palpating a sausage-shaped mass, which contracts and expands beneath the fingers' (Pearson and Wyllie).

The question of whether a tumour can be palpated or not is of great importance. Success obviously depends upon the skill of the examiner, the time and conditions under which the examination is carried out, and the position of the mass. Still (1921), in common with many successful paediatricians, believed that the child's abdomen should be palpated during sleep. Clubbe (1906, 1921) who had a very considerable experience of intussusception, said that, 'if there is any distension, or if the child resists or screams, it is quite hopeless

to expect to find a mass in the abdomen, even though there be a large one.' He believed that an anaesthetic 'should always be given for diagnostic purposes whenever you fail to feel a tumour, even though the child did not seem to resist your manipulation in any way.'

No one can seriously doubt the value of a properly conducted clinical examination, yet it seems that it is seldom performed efficiently, for in a series of sixty-two cases collected from the literature, a tumour was detected **at some time** in only forty-seven. In many cases, the child has suffered for months, and in not a single instance was the child examined under an anaesthetic.

Radiology offers another approach to the problem of how to detect the mass. Some experienced workers, notably Nordentoft (1939) in Denmark, believe that radiography is reliable in a high proportion of cases. A barium enema is the usual procedure. Generally, the examination can be made quickly and easily without undue stress to the patient, but it is essential that it should be complete and thorough (for Nordentoft has emphasized that intussusception can never be excluded unless the enema is seen to flow through the ileocaecal valve into the small bowel). Once the intussusception is visualized the diagnosis is not difficult, since the radiographic features are well known and quite distinctive. Occasionally the examination fails because the child will not take a full enema, but in such cases a child may be given an anaesthetic. In about five per cent. of cases the intussusception is of the enteric variety and in such cases a barium enema is negative, but preliminary films of the abdomen may show abnormal gaseous distension of a coil or coils of small bowel, and when necessary, the diagnosis can be confirmed by a barium meal (subject to there being no clinical indication which would render a barium meal inadvisable).

In the light of the experiences reported here it is urged that the only reliable clinical feature is a story of repeated attacks characterized by the sudden onset of gripping abdominal pain. All other symptoms of intussusception may be absent and are unreliable. A suspicious case should be carefully examined until the observer is satisfied that the whole abdomen has been carefully palpated; if necessary an anaesthetic should be given to secure proper relaxation. Likewise (sometimes in preference to examination under anaesthesia), the child should be submitted for a careful radiographic study of the alimentary canal, preferably begun with a preliminary film of the abdomen and a barium enema, but supplemented, when negative, by a barium meal. The clinician must remember that unless the radiologist has sufficient time to make himself familiar with the clinical picture, the radiological examination is unlikely to prove reliable on all occasions.

Summary

(1) Three cases of chronic intussusception in children are described. In two cases, the condition was not suspected for a long time owing to the apparent absence of a palpable abdominal tumour, and in the third case because the tumour did not persist.

(2) The common features in the histories of these cases were repeated attacks characterized by the sudden onset of central abdominal pain.

(3) Any child who gives a suggestive history should be carefully examined, for owing to the difficulty in securing proper relaxation the tumour can be very easily missed.

(4) Radiological studies should be made whether a tumour is palpable or not, but it is essential that the examination should be thorough.

Thanks are due to Dr. A. Cooke, Professor L. Findlay, and Professor L. J. Witts for their kind permission to record these cases, and Mr. D. C. Corry for his notes on the operative findings. Professor Findlay has kindly assisted by criticising the manuscript.

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APPENDIX
PREVIOUS CASE REPORTS OF CHRONIC INTUSSUSCEPTION

Author	Age	Length of history	Acute onset noted	Abdominal pain	Vomiting	Bowel habit	Blood in faeces	Wasting	Tumour	Remarks
Medical Annotation (1873). *Lancet*, **1**, 709.	$\frac{6}{12}$ yr.	3 wk.	–	N.M.	N.M.	Diarrhoea	–	N.M.	–	Lump felt by mother. None found by doctor. Died
Dr. Chaffey (1888). *Lancet*, **2**, 17.	3 yr.	? 6 wk. ? 10 days	–	+	+	Constipated	+	+	+	
T. A. McGraw (1897). *Brit. med. J.*, **2**, 956.	7 yr	$\frac{4}{12}$	+	+	+	Diarrhoea or regular	+	+	–	
G. A. Wright and K. Renshaw (1897). *Brit. med. J.*, **1**, 1470.	2 $\frac{10}{12}$ yr.	4 wk.	–	–	–	Constipated	–	N.M.	–	
Bernard Pitts (1897). *Lancet*, **1**, 1602.	2$\frac{3}{12}$ yr.	1$\frac{1}{2}$ yr.	+	+	+	Constipation or diarrhoea	+	+	+	Recurrent type
F. G. Penrose and T. H. Kellock (1898). *Lancet*, **2**, 261.	1$\frac{4}{12}$ yr.	3 wk.	+	+	+	N.M.	–	–	+	
F. Eve (1899). *Clin. J.*, **14**, 273.	13 yr.	3 wk.	+	+	+	Constipated	+	N.M.	–	'A tumour is felt in about 50 per cent. of cases'
F. P. Connor (1903). *Lancet*, **2**, 600.	9 yr.	1 mth.	+	+	+	Constipated	once	N.M.	–	Diagnosed subacute appendicitis or 'tuberculous mischief.' There was an indefinite resistance on abdominal palpation
R. G. Hogarth (1903). *Brit. med. J.*, **1**, 854.	6 yr.	5–6 wk.	–	+	+	Diarrhoea or regular	–	+	+	Not felt on May 12th in O.P. Felt on admission on May 22nd
C. H. Fagge (1904). *Ann. Surg.*, **41**, 407.	9$\frac{6}{12}$ yr.	24 days	–	+	+	Irregular	N.M.	–	+	Despite mass, Tub. peritonitis diagnosed at first. Died 5$\frac{1}{2}$ hr. after operation
	2$\frac{8}{12}$ yr.	3 wk.	–	+	–	N.M.	+	N.M.	+	Felt P.R. only. Treated 3 wk. as dysentery. Died 5 hr. after operation
G. E. Waugh (1911). *Lancet*, **1**, 1492.	2 $\frac{11}{12}$ yr.	2–3 wk.	–	+	+	N.M.	–	N.M.	+	Penile pain
	2$\frac{6}{12}$ yr.	2 wk.	–	+	+	Regular	–	+	+	Not felt for 5 days. Penile pain
	3 yr.	6 days	–	+	+	? Regular	–	N.M.	+	Penile pain
T. B. Henderson (1912). *Brit. med. J.*, **2**, 761.	1$\frac{1}{12}$ yr.	6 wk.			–	Diarrhoea			–	? recurrent acute intussusception
J. P. Buckley (1919). *Brit. med. J.*, **2**, 665.	2 yr.	5–6 wk.	N.M.	N.M.	Yes	Diarrhoea	No	+	+	Superimposition of retrograde upon direct intus-

J. P. Buckley (1919). *Brit. med. J.*, **2**, 665.	2 yr.	5–6 wk.	N.M.	N.M.	Yes	Diarrhoea	No	+	+	Superimposition of retrograde upon direct intussusception
F. M. Spencer (1920–1). *Brit. J. Surg.*, **8**, 366.	$7\frac{1}{2}$ yr.	4 mth.	–	+	+	Constipated at first	+	+	+	Indefinite mass. Treated as abdominal tuberculosis for 6 wk. Still believed to be so at operation; had ascites. Died 36 hr. after operation
G. F. Still (1921). *Arch. Pediat.*, **38**, 174.	$1\frac{2}{12}$ yr.	6 wk.	+	+	+	Constipated	Trace	+	+	Only one attack of pain
	$1\frac{11}{12}$ yr.	32 days	+	+	+	Loose	Trace	+	+	3 of the 4 cases were previously diagnosed as ? Tub. Peritonitis
	$\frac{13}{12}$ yr.	32 days	–	+	+	Regular	Trace	+	+	
	$3\frac{6}{12}$ yr.	21 days	+	+	+	Regular	Trace	+	+	
H. H. Schlink (1922). *Med. J. Aust.*, **1**, 270.	7 yr.	2 mth.	+	+	+	Diarrhoea	–	+	+	Felt after 5–6 weeks
J. B. Alexander (1923). *Brit. med. J.*, **1**, 508.	4 yr.	12 days	+	+	+	Regular	+	–	+	
R. C. Dun (1923). *Brit. med. J.*, **1**, 107. (10 cases.)	Average 5 yr.	4 wk.–$2\frac{1}{2}$ yr. yr.	–	N.M.	N.M.	N.M.	2 cases + 8 cases –	N.M.	+ in 6 cases – in 4 cases	Symptoms not discussed
J. Gaymer Jones (1924–5). *Brit. J. Surg.*, **12**, 378.	7 yr.	2 wk.	–	+	N.M.	Normal	+	N.M.	+	Due to submucous lipoma supervention of acute on chronic intussusception
	12 yr.	2 wk.	–	+	+	Normal	–	+	+	Tumour in R.I.F., not tender. Possibly intussusception due to appendicitis
	$\frac{8}{12}$ yr.	1 mth.	–	N.M.	+	Diarrhoea and constipation	+	+	+	Not felt one day but felt the next
	$\frac{11}{12}$ yr.	8 days	+	+	+	Constipated at first	+	+	+	' Acute on chronic '
	9 yr.	2 wk.	–	+	–	Regular	–	N.M.	+	
	5 yr.	Pain 6 wk. ago then free until 1 wk. ago	–	+	N.M.	Regular	–	+	+	
A. W. Owen (1924). *Brit. med. J.*, **1**, 904.	6 yr.	4 wk.	+	+	+	Regular	–	+	+	Not felt for 26 days
H. E. Marsh (1924). *Ann. Surg.*, **79**, 244.	$2\frac{1}{2}$ yr.	10 wk.	+	+	+	Constipated	+	+	–	' Not felt as child was crying '
	3 yr.	10 wk.	–	+	–	Constipated	–	–	–	
J. S. Stone (1925). *Boston med. surg. J.*, **192**, 210.	3 yr.	6 wk.	–	+	N.M.	N.M.	+	N.M.	' Doubtful tumour '	
	$2\frac{1}{12}$ yr.	9 mth.	–	N.M.	N.M.	Constipated	–	N.M.	+	' Intussusception had sloughed off, leaving area of obstruction and ulceration '
	2 yr.	1 mth.	–	+	N.M.	Regular	+	N.M.	+ Felt after 1 mth. in hospital	

N.M.=Not mentioned

PREVIOUS CASE REPORTS OF CHRONIC INTUSSUSCEPTION—*continued*

Author	Age	Length of history	Acute onset noted	Abdominal pain	Vomiting	Bowel habit	Blood in faeces	Wasting	Tumour	Remarks
J. F. H. Stallman (1926). *Ann. Surg.*, **84,** 735.	$\frac{9}{12}$ yr.	2 mth.	—	+	+	Normal	+	—	+	
	11 yr.	2 mth.	+	+	+	Diarrhoea in attacks	+	+	+	
	$\frac{6}{12}$ yr.	$3\frac{1}{2}$ mth.	—	+	+	Constipated	+	+	+	
	5 yr.	9 wk.	—	+	+	Constipated	+	—	+	
	7 yr.	3 mth.	+	+	+	Alternating diarrhoea and constipation	—	+	+	Tub. peritonitis diagnosed. Post mortem intussusceptiion and general peritonitis
	$\frac{7}{12}$ yr.	5 wk.	—	+	+	Slight diarrhoea	+	+	+	
	$\frac{8}{12}$ yr.	3 wk.	+	+	+	Constipation, later diarrhoea	+	N.M.	—	'Tumour not noted in case report'
	$\frac{2}{12}$ yr.	2 wk.	+	+	+	Diarrhoea at first	—	—	+	
	2 yr.	3 wk.	—	+	+	Constipation at first, later diarrhoea	+	+	+	
H. B. Epstein (1927). *Amer. J. Surg.*, **3,** 262.	2 yr.	3 mth.	N.M.	+	N.M.	—	Trace	N.M.	—	
O. B. Markey and K. Kato (1927). *Amer. J. Dis. Child.*, **34,** 249.	$\frac{3}{12}$ yr.	5 mth.	+	+	+	Constipated	+	+	+	Intussusception prolapsed through anus
E. J. Donovan (1928). *Amer. J. Surg.*, **5,** 274.	$\frac{15}{12}$ yr.	2 mth.	+	+	+	Constipated	+	+	+	Intussusception protruded at anus
P. W. Beaven (1929). *Amer. J. Dis. Child.*, **37,** 373.	3 yr.	5 wk.	+	+	—	Regular	—	—	—	Inverted Meckel's diverticulum
	5 yr.	13 days	+	+	—	Constipated	—	—	—	Penile pain
D. M. Sutherland (1932). *Arch. Dis. Childh.*, **7,** 191.	3 yr.	2 mth.	—	+	—	Constipated	—	+	+	Original diagnosis tuberculous mesenteric glands
C. W. Mayo (1933). *Proc. Mayo Clin.*, **8,** 313.	$3\frac{6}{12}$ yr.	5 wk.	—	+	+	Constipated	—	—	+	P.R. mass suspected
J. R. Ryan (1936). *Med. J. Aust.*, **2,** 331.	$\frac{7}{12}$ yr.	6 wk.	+	+	+	Regular or diarrhoea	+	+	+	Chronic and retrograde intussuception

N.M. = Not mentioned

CARDIAC COMPLICATIONS IN SCARLET FEVER

BY

C. NEUBAUER

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Involvement of the heart is not an uncommon complication in scarlet fever. A large amount of clinical material has encouraged this review of the problem of cardiac complications in scarlet fever and in related haemolytic streptococcal infections.

Stegemann (1914) described pathological changes in the myocardium and nervous system of the heart. Siegmund (1931) found inflammation chiefly in the thebesian vessels. Brody and Smith (1936) found pathological changes in the heart of 90 per cent. of the fatal cases. They described three types of myocarditis: 1. Focal or diffuse interstitial myocarditis. 2. Arteritis or periarteritis of the smaller coronary arteries. 3. An infiltration of the coronary veins or of the endocardium of the ventricles. Albert (1938) found myocarditis in four cases among eight children who died of scarlet fever. Toomey (1942) found haemorrhages in the bundle of His in a case of auriculo-ventricular block. Five cases of double infection of scarlet fever and diphtheria were examined by the same author: myocarditis was found in two cases.

Among the clinical reports Nobécourt's paper (1918) must be mentioned; he found two out of seven soldiers who had clinical signs of endocarditis and developed signs of permanent damage in the heart. Thursfield (1929) found carditis especially in cases of scarlet rheumatism and he noticed permanent damage in some of the cases. The cardiac complications due to scarlet fever without scarlatinal rheumatism are regarded by him as temporary and he did not see permanent damage in these cases. Rolleston (1912) noticed a fall in blood pressure in 25 per cent. of the cases after an initial rise in the beginning of the disease. He found (1929) the incidence of endocarditis below one per cent.; myocarditis was more common and this was manifested by rapid and small pulse, feeble heart sounds and gallop rhythm, but no data of its incidence could be given. Stoeber (1935) described his main clinical findings in myocarditis in scarlet fever as: cardiac enlargement, soft systolic apical murmur and arrhythmia. He attributed sudden death in scarlet fever to an acute myocarditis. Wyborn (1934) out of a series of 2,300 cases at the South Eastern Hospital discovered only four cases of arrhythmia, one being a case of auricular fibrillation and the other three just simple arrhythmia. Out of 600 cases of scarlet fever Faulkner (1935) had seven that developed signs of chronic valvular disease. In two of his cases the signs of endocarditis developed in hospital before discharge. Harries and Mitman (1944) regard the carditis in scarlet fever as identical with that of acute rheumatic fever: in their opinion it is an endocarditis which leaves permanent valvular lesions. Cardiac enlargement was observed by Toomey (1942) in five per cent. of his cases and heart block has been seen in one case during life.

In the present study clinical examination, cardiogram, x-ray photograph and blood sedimentation rate were taken into consideration in arriving at the conclusion whether a heart complication was present or not. The children with a cardiac complication were kept under observation for a period of at least one year after the onset of the acute disease to ascertain the occurrence or non-occurrence of permanent cardiac damage. An attempt was made to differentiate cases of myocarditis from those with endocarditis and from others in which both conditions were present.

Incidence

There are 602 cases of scarlet fever in the present series observed from August, 1943, till August, 1944. In the majority of the cases the disease was generally of a mild character. On the average cases were discharged during the fourth week of disease. The mild character of the disease can be judged by the incidence of complications occurring. Apart from cardiac complications these were:

Otitis media	18 cases	3 per cent.
Mastoiditis	5 cases	0·8 „ „
Purulent rhinitis ..	68 cases	11·2 „ „
Adenitis	57 cases	8·1 „ „
Scarlatinal rheumatism	4 cases	0·6 „ „
Nephritis	3 cases	0·5 „ „

There were in addition 36 cases of cardiac complication recorded in the present series, that is an incidence of 5·9 per cent.

The ages of the patients with carditis were:

0–10 years	25 cases
Over 10 years	11 cases

The history: None of the patients with a cardiac complication had a history of a previous attack of acute rheumatic fever. This is of some importance, because an infection with S. haemolyticus could easily elicit a flare-up of a latent rheumatic carditis.

Ten of the children, however, had had one acute infectious disease previously, twelve had had two infectious diseases, nine had had three, whilst one child had had four and another five infectious diseases within the last two or three years. Three patients had had no disease before.

The diseases concerned were:

Measles	30 cases
Pertussis	13 cases
Chickenpox	12 cases
Rubella	6 cases
Mumps	4 cases
Repeated tonsillitis	4 cases
Bronchopneumonia	5 cases

Clinical findings

The heart on admission: Ten cases amongst those who developed carditis in the course of the disease exhibited a marked tachycardia on admission; a soft systolic murmur was audible at the apex in five cases and over the heart base in one case.

Onset of carditis: In more than half of the cases of the present series, the cardiac complications were discovered in the second or third week of the disease. The child was often almost ready for discharge when the first clinical signs were observed.

The onset was observed:

Within the first 10 days of disease	5 cases
From 11th–20th day of disease	16 cases
From 21st–30th day of disease	12 cases

Faulkner (1935) examined 171 cases of scarlet fever cardiographically and he could not find any abnormality before the thirteenth day of disease. Such has not been my experience for, in five instances, I found the onset of carditis within the first ten days. As has been reported on another occasion, a myocarditis re-occurs readily in a child who has had a myocarditis previously, especially in a child with a history of several infectious diseases within the last one or two years. In children, however, who had no previous infectious disease or who had one a long time ago, the myocarditis manifests itself towards the end of the second, more often in the third or fourth week of the disease.

This is of some importance:

1. The carditis follows the tonsillitis after a certain interval as in acute rheumatic fever.
2. The carditis occurs at a time when the patient is commonly regarded as being fit to get out of bed.

General signs. Pallor, listlessness, slight cyanosis may be the first signs to indicate a cardiac involvement. The eyes are shadowed. The slightest effort may cause fatigue.

Clinical signs.

MURMURS are frequent in children and little reliance can be placed upon them. It is well known that a high temperature or a severe anaemia may be the cause of an apical systolic murmur. In the present series murmurs manifested themselves in the course of the disease as follows:—

Mitral systolic murmur, which disappeared	16 cases
Mitral systolic murmur which became permanent	2 cases
Mitral presystolic murmur which became permanent	2 cases
Cases admitted with systolic murmur, which was permanent	6 cases

A murmur may disappear and become manifest again. Findlay (1931) in his comprehensive paper on rheumatic infection in childhood found that in a proportion the murmur returned after a period of years. It would be equally wrong to attribute some importance to each murmur as it would be, for example, to disregard all systolic murmurs at the apex. The difficulty lies in the fact that it is not possible to differentiate an organic from a functional murmur on clinical grounds alone; experience has shown that there are good reasons to suspect a carditis if the murmur at the apex is loud and if it has a wide transmission or if a diastolic or presystolic murmur manifests itself.

CARDIAC ENLARGEMENT. A definite enlargement of the cardiac dullness is an important sign of acute carditis. Owing to the enlargement the apex beat is displaced either outward, or outward and downward. This is not a common finding, however, especially in an early case, and it was found in only three cases in the present series. The cardiac dullness is only a little increased in most cases. It will be shown that the cardiac disease occurring in scarlet fever is due as a rule to myocarditis rather than to a valvular disease. Persistent tachycardia, diminished intensity of the first apical sounds are signs of a myocarditis in the early stages of the disease, whereas changes in the rhythm like gallop rhythm or embryocardia occur more frequently in advanced stages. In the present series the first apical sound became markedly diminished in intensity in seven cases; the first apical sound became equal in intensity to the second in two cases; frequent premature beats were found in another case.

The clinical signs subsided after a shorter or longer period:—

Within 3–4 weeks	in 8 cases
,, 5–6 weeks	,, 6 cases
,, 7–8 weeks	,, 8 cases
,, 9–10 weeks	in 8 cases
After 3 months	in 2 cases
,, 6 months	,, 1 case
,, 7 months	,, 1 case

In some instances, however, a presystolic murmur may persist, it may become an early diastolic murmur later on and a late diastolic murmur after several months. Two cases of this kind have been observed in the present series. In two more cases a mitral systolic murmur developed which became permanent.

THE TEMPERATURE. An increase in temperature after an afebrile period was noticed in seven cases. Clinical signs of carditis were found simultaneously with the increase of the temperature in four cases; the temperature preceded the clinical signs in three cases, whilst the carditis was noticed a few days

before the temperature rose in three more cases. The febrile period lasted:—

3 days in 2 cases
4 „ „ 2 cases
6 „ „ 1 case
9 „ „ 1 case

THE BLOOD PRESSURE. In diphtheria and typhoid fever myocarditis is nearly always accompanied by a considerable fall in pressure. This is, however, not the case in scarlet fever. Rolleston (1912) found a fall in blood pressure in 25 per cent. of the cases after an initial rise during the febrile period. In the present series the diastolic pressure was found lowered in fourteen cases (38 per cent.), systolic and diastolic pressure was diminished (22 per cent.) in eight cases.

From the signs and symptoms enumerated so far it becomes clear that it is difficult to state whether an acute carditis is present in a case of scarlet fever or not, and why the clinician, because of the absence of recognizable clinical signs of carditis, is often reluctant to accept its diagnosis.

THE BLOOD SEDIMENTATION RATE (B.S.R.). The B.S.R. has been proved to be a test of great value in determining whether a heart disease is acute or not, and in estimating the degree of activity of a cardiac lesion. It stands to reason that an infection with S. haemolyticus might cause an increase of the B.S.R. but the increase in the B.S.R. is greater in a case complicated by carditis than in an uncomplicated case of scarlet fever.

The figure on the left (see fig. 1) shows the curve according to the original Westergren method taken

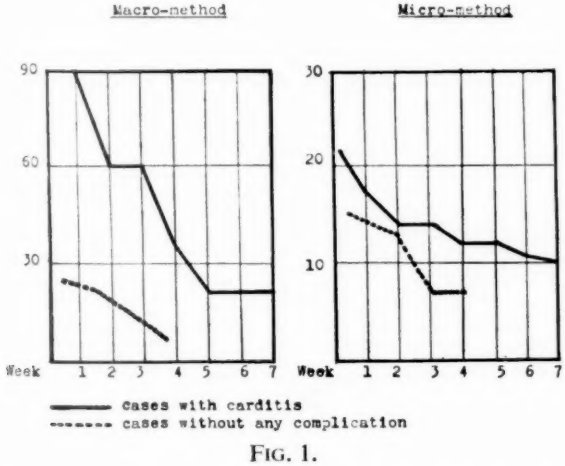

FIG. 1.

from ten cases of carditis, the B.S.R. being 90–100 in the first hour during the first week of the disease, dropping to about 25 after six to seven weeks. The dashed line shows the B.S.R. in ten cases of scarlet fever without any complication taken by the original Westergren method. The difficulty encountered with the Westergren method is that it is not always easy to obtain blood from a child by venaepuncture. Therefore a micromethod was found more convenient, as blood flowing freely from a punctured finger is more easily obtainable. The figure on the right shows a curve, the average B.S.R. of 29 cases of carditis in scarlet fever taken by micromethod. Compared with the first curve it shows that during the acute stages of the carditis the macromethod is more sensitive, giving higher readings. A micromethod for B.S.R. has been used by Cutler (1927), Smith (1936), Benson and Rogers (1941), Trought (1942). It is of definite value in estimating the clinical condition in scarlet fever. It was increased in all instances but two, when the readings were doubtful. But by tests repeated at intervals a useful indication is given of the progress of the carditis. A sudden increase in the B.S.R. over 50 by macromethod or 20 by micromethod is a danger sign, which must not be ignored. The increase of the B.S.R. was found highest in the first and second week of the carditis. It dropped during the third week, remained for a week or so on the same level with either method and dropped in the course of the fifth week, but it was still increased during the sixth or seventh week. In some instances it remained increased for months as in rheumatic heart disease. The dashed line in the right figure shows the B.S.R. of twenty-nine cases of scarlet fever without any complication taken by micromethod. Technical errors can be made with either method. In agreement with Trought it was found that the normal readings of the B.S.R. by micromethod were 2–9 mm. in the first hour. It was found increased up to 14 mm. in moderately severe cases of carditis and up to 30 mm. in very acute cases of carditis.

THE CARDIOGRAM. The increasing use of the cardiograph has lead to rapid advances in knowledge of the diseases of the heart; it is an objective method of examining the heart function. Without a cardiogram an examination of a child's heart cannot be regarded as complete.

The cardiograph was used for investigations in fifty scarlet fever patients first by Shookhoff and Taran (1931). They found changes in the S–T segment in 14 per cent. of the cases and the T wave in 10 per cent. They found furthermore that all abnormalities disappeared in early convalescence. Faulkner et al. (1935) examined by cardiograph 171 scarlet fever cases from 1932–1934 during a relatively mild endemic. They found abnormal records in eleven cases (6 per cent.). The auriculoventricular conduction was prolonged in five cases and T wave changes were found in six cases. The T wave changes consisted of marked temporary diminution in amplitude or flattening or inversion.

Cardiograms are not taken in this hospital as a routine, but only if heart disease is suspected. In other words, this study is based on a group of patients who have been selected on the basis of suspected heart disease. In such a case one or more cardiograms were taken during the acute stage of the disease, another during convalescence and in those instances in which recovery was incomplete, the patient was followed up by examinations in monthly or longer intervals after discharge. The common findings in the cardiogram of a carditis were: 1. The deviation of the S-T segment. 2. The

flattening or inversion of the T waves. 3. The voltage of the ventricular deflections was diminished especially in advanced cases of myocarditis. As pointed out before, serial records may be necessary to detect the presence of a carditis. In addition impairment of the auriculo-ventricular conduction manifested by prolongation of the P–R interval occurred, leading to partial A-V block (see case 3, p. 86). The cardiogram may show P–R prolongation without other abnormal findings (see case 4). Frequent premature beats have been observed (see case 5) and also auricular fibrillation (see case 7). Increase in size, notching and widening of the P waves occurred frequently (see cases 2, 5, 6). Following recovery the cardiogram usually returned to normal. This happened in milder cases within six weeks (see case 1): in moderately severe cases within two to three months (see case 2). It is often the best evidence of the subsidence of the active stage of the carditis and in general the patient should not be allowed to get up until the cardiogram has become normal. Occasionally, however, pathological changes may persist or become even more intense after discharge. It is obvious that clinical, cardiographic and laboratory findings have to be correlated to decide whether or not heart disease is present, when it has passed from the acute into the subacute stage and when it has subsided altogether. The diagnosis of a carditis was confirmed by cardiogram in thirty-six cases in the present investigation. There were:—

33 cases of myocarditis
2 cases of partial A-V block
1 case of auricular fibrillation

The incidence of myocarditis is still disputed. There are clinicians who regard it as common and not particularly serious; there are others who find it a rare clinical condition and of great importance. Our investigations show that myocarditis is not an uncommon complication in scarlet fever and its prognosis is uncertain.

X-RAY EXAMINATION. Examination by x-rays is of great value in determining changes of the size, shape and position of the heart. In some instances it shows enlargement of the heart during the acute stage of the disease, but the enlargement is not well marked. When a permanent valvular damage results the x-ray photograph after several months shows more definite changes, e.g. prominent right border of the heart or a mitral bulge (see cases 6 and 7).

Treatment

The most important item in the treatment of carditis is to spare the heart unnecessary work. It is advisable to send the child to hospital, if possible. Complete rest should be given and bed-rest continued until the pulse becomes normal, the B.S.R. reaches a normal level and the abnormalities in the cardiogram subside. In doubtful cases it is better to be on the safe side and keep the child in bed a little longer. With prolonged bed-rest the myocarditis will probably subside. Treatment of the original disease with serum, sulphonamide or both has no effect on the complications in scarlet fever. In the present series seven patients received serum, fifteen patients sulphonamide, and two both serum and sulphonamide. Twelve children had no treatment. There can be little doubt that serum treatment has no special influence on the incidence of heart complications.

According to the annual report of the M.O.H., Newcastle upon Tyne, for 1938, there were 662 cases of scarlet fever; 178 were treated with serum, the incidence of complications was 27 per cent. with 0·6 per cent. cardiac complications; 484 cases were treated without serum, the incidence of complications being 28·9 per cent. with 0·2 per cent. cardiac complications. The same applies to treatment with sulphonamides. French (1939) used doses of 5 gm. daily for fourteen days and 3 gm. daily for the next fourteen days in a carefully controlled investigation in Glasgow. He found no effect on the complications. Wesselhoeft (1942) citing the combined results of four clinical investigations to find out the value of sulphonamide for the prevention of complications in scarlet fever observed no diminution in the incidence of complications among 474 treated cases compared with 587 controls. Furthermore, a combination of the drug with scarlet fever antitoxin in 317 cases brought no diminution in the incidence of complications compared with a similar group of 329 cases treated with serum alone.

The original disease in the present series of thirty-six cases of carditis was mild or moderately severe. This shows the incidence of other complications:—

Adenitis	3 cases
Purulent rhinitis ..	2 cases
Otitis media	2 cases
Nephritis	1 case
Scarlet rheumatism ..	2 cases

One child died of a double infection with S. haemolyticus and C. diphtheriae on the fifteenth day of disease. The post-mortem examination revealed an acute interstitial myocarditis involving both auricles and both ventricles.

Convalescence

Experience has shown that the majority of scarlet fever patients make a complete recovery; adolescents and adults often put on weight to such a degree that it exceeds their weight before the illness. In contradistinction to these patients there is another group of children who make a slow recovery and the condition of some of them deteriorates after discharge from hospital. These children are pale, they look anaemic, their appetite is poor, they always feel cold and they easily become tired. Some of them are restless, they do not sleep well; others easily become breathless when going upstairs. Some have a good colour, but they lose it after the slightest effort. The appearance of a slight oedema on the dorsum of the feet is not uncommon. These symptoms and signs have often not been understood and have been misinterpreted as 'secondary' or 'post-infectious' anaemia. The blood investiga-

tion reveals a hypochromic normocytic anaemia in many instances, but this is one sign of the disease and not the disease itself. In the present investigation these children with cardiac disease were followed up after their discharge from hospital and it was found that the carditis which originated during the acute illness was still present or became even worse after discharge from hospital. The children were brought to the hospital for examination in response to a letter requesting their parents to do so. They can be divided into three groups:—

1. Those who make a complete recovery after several months; the clinical signs subside and the cardiogram returns to normal (see case 1).
2. Those who become better, but the cardiogram shows abnormalities (see case 6).
3. Those who develop a valvular lesion (see case 5).

There were twenty-nine cases belonging to the first group, two belonging to the second group and four belonging to the third group in the present series of thirty-six cardiac complications.

These investigations show that the cardiac complications occurring in scarlet fever are due in great part to myocardial damage. The total incidence, twenty-nine cases out of 602, was 4·8 per cent. There do not appear to be any reports about the incidence of myocarditis in scarlet fever.

Saphir et al. (1944) in a most comprehensive paper on myocarditis in children found 97 cases of myocarditis amongst 1,420 autopsies of children between the ages of eight days and sixteen years. The incidence was 6·8 per cent. Vischer (1924) found twenty-seven cases of myocarditis in 793 autopsies of children, i.e. 3 per cent. However, as the material investigated by these workers came from general paediatric hospitals, it did not contain many cases of acute infectious disease and their results can not be compared with the present findings.

The incidence of endocarditis in scarlet fever has been studied by several clinicians: Broadbent (1909) found an incidence of 1·8 per cent.; Nobécourt (1918) 2·5 per cent.; Joe (1924) 0·25 per cent.; Rolleston (1929) less than 1 per cent.; McCollum (1925) 1·8 per cent.; Faulkner (1935) 1·1 per cent. The incidence of endocarditis in the present series was 0·66 per cent.

The clinical and cardiographic findings in endocarditis in scarlet fever are similar to those in acute rheumatic heart disease. Although the etiology of acute rheumatic fever is not known, it is well established that S. haemolyticus is frequently associated with acute rheumatic fever. Many investigators believe that S. haemolyticus is etiologically important and possibly the actual cause of the disease. Others have expressed the view that the pathological changes in rheumatic fever are the result of allergy to S. haemolyticus (Swift, Derick, Hitchcock, 1928; Klinge, 1933). The diseases show the following similar points: Sore throat at the onset; carditis manifests itself after two or three weeks, if at all; arthritis common in rheumatic fever, occasional in scarlet fever; increased B.S.R.; the cardiographic and x-ray findings are similar. There is, however, one difference: Aschoff's bodies, accepted by most investigators as specific lesion of acute rheumatic heart disease, have not been seen by the authors mentioned above.

Nowadays scarlet fever is generally regarded as a mild disease, which it certainly is according to the course the disease runs in the majority of the cases and its low mortality. The present investigation shows, however, that heart disease might be acquired in childhood in the course of a mild scarlet fever. It shows, furthermore, how useful it is to see the patient from time to time after his discharge from hospital to ascertain whether the cardiac damage is permanent or not.

ILLUSTRATIVE CASES

Clinical data and cardiographic findings

Case 1. A. B., 16 years. Stay in hospital: 11 weeks. Previous disease: Measles.

ON ADMISSION: Severe tonsillitis, rash, C. diph. negative, S. haemol. positive. Nephritis on the 22nd day of disease. Carditis on the 29th day of disease. Persistent tachycardia, rough systolic apical murmur. B.S.R. 70 mm. in the first hour (macromethod). Discharged with systolic murmur over the heart base and apical region.

CARDIOGRAPHIC FINDINGS: (fig. 2).

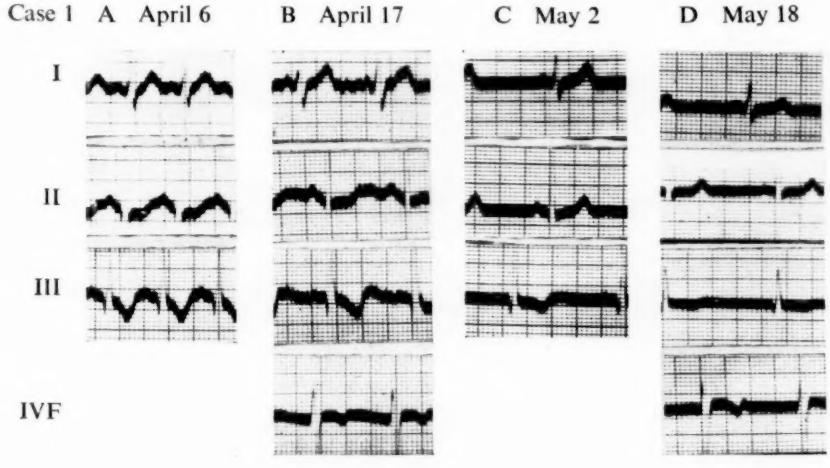

FIG. 2.

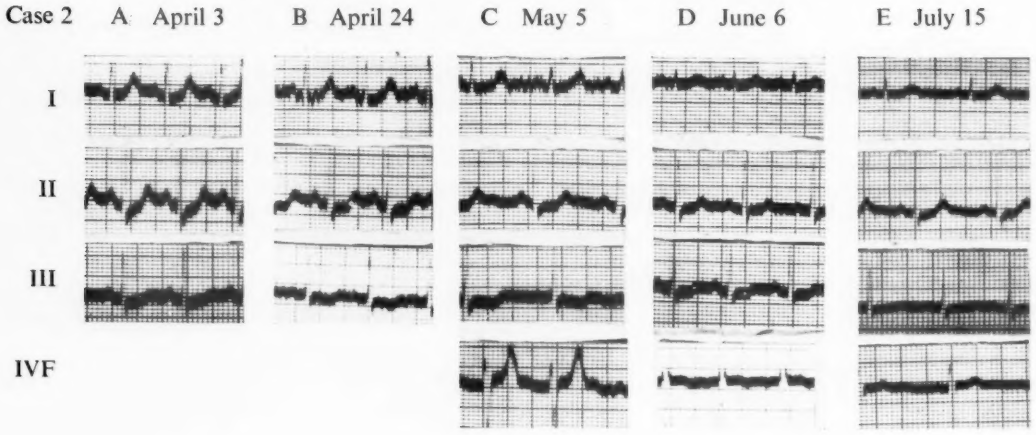

FIG. 3.

RECORD A: Sinus tachycardia, ventricular rate 136 per minute. Right axis deviation, S–T segment below the base line in lead II and III. T diphasic in lead II, T inverted in lead III.

RECORD B: Taken eleven days later, shows more marked right axis deviation, S–T segment dislocated in lead II and III. T wave diphasic in lead II and inverted in lead III and lead IV.

RECORD C: Taken one month after the onset of the carditis: Right axis deviation T wave upright in lead II and less inverted in lead III.

RECORD D: Taken seven weeks after the onset of the carditis, the right axis deviation is subsiding and the findings are normal. A diphasic T wave in lead IV may be seen in healthy adolescents.

Case 2. A.G., 12 years. Stay in hospital: 46 days. Previous diseases during the last three years: measles, chickenpox, pertussis, pneumonia. On the 12th day of disease cardiac signs, enlargement of the cardiac dullness, systolic apical murmur. Four weeks after discharge, pale, easily tired, 'weak in the ankles.'

CARDIOGRAPHIC FINDINGS (fig. 3).

RECORD A: Sinus tachycardia, ventricular rate 150 per minute. S–T transition below the base line in all three leads. P wave peaked in lead II.

RECORD B: Taken three weeks later. Ventricular rate 120 per minute. S–T segment below the base line in lead II and III. P wave peaked in lead II. T waves have become smaller.

RECORD C: Taken one month after onset of the carditis. S–T segment below the base line in lead II and III. T wave small and round in lead II. T inverted in lead III.

RECORD D: Taken two months after the onset of the carditis, shows the S–T segment depressed in lead I and II, S–T below the base line in lead III, T wave has become flatter in lead I, smaller in lead II and diphasic in lead III. The QRS is down and the T wave inverted in lead IV.

RECORD E: Taken four months after the onset of the carditis: S–T still below the base line in lead II and III. S–T depressed in lead I. The T wave has become upright in lead IV.

Case 3. J. M., 11 years. Stay in hospital 35 days. Previous diseases: measles, pertussis. Signs of carditis on the 27th day of disease, systolic apical murmur, highly increased B.S.R. Two months later: easily tired, 'weak on his legs.' Apical murmur less intense.

CARDIOGRAPHIC FINDINGS (fig. 4).

RECORD A: P–R 0·27 second. S–T depressed in all three leads. Partial A-V Block of first degree.

RECORD B: Taken five days later, shows a P–R interval of 0·24 second.

In RECORD C, taken three weeks after the onset of the carditis, the P–R interval is normal. S–T segment depressed in lead II, the T wave has become flat in lead II and inverted in lead III.

RECORD D: A follow-up examination two months

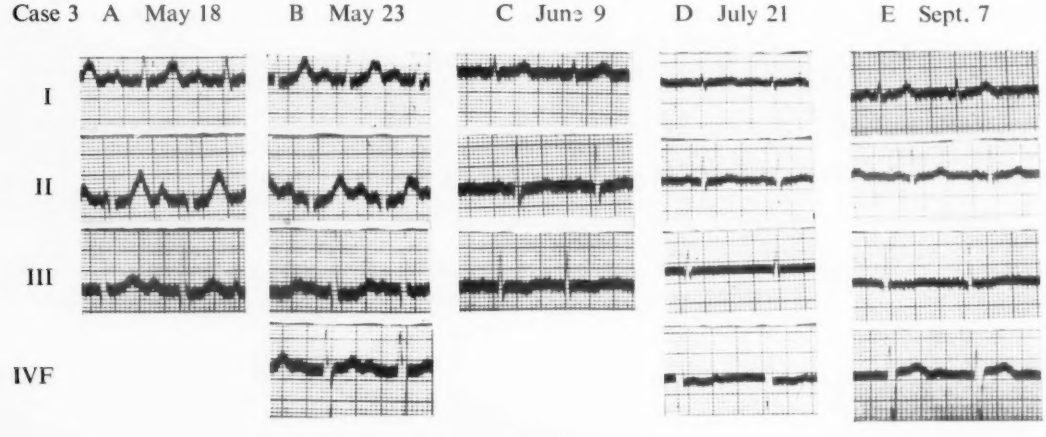

FIG. 4.

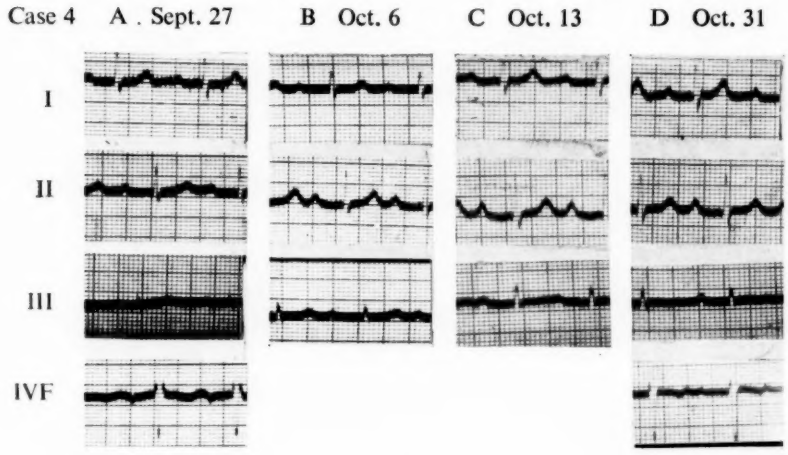

FIG. 5.

after the onset of the carditis. The voltage of QRS has become diminished, 1·2 mV in all three limb leads together S–T transition depressed in lead II. The T wave has become flat in lead I and inverted in lead IV QRS of Q type in lead IV.

RECORD E: Taken four months after the onset of the carditis is normal.

Case 4. B. M., 15 years. Stay in hospital 40 days. Previous diseases: chicken-pox and measles. Onset of carditis on the 18th day of disease: presystolic apical murmur, high B.S.R.

CARDIOGRAPHIC FINDINGS (fig. 5).

RECORD A: P–R. 0·27 second. No other sign of myocarditis.

RECORD B: 31st day of disease: P–R. 0·30 second.

RECORD C: Three weeks after the onset of the carditis. P–R. 0·32 second.

RECORD D: Taken three weeks later. P–R. 0·29 second.

Case 5. S. F., 11 years. Stay in hospital 54 days. Previous diseases: measles, chickenpox, otitis media. Signs of carditis on the 13th day of disease: systolic apical murmur, frequent premature beats. Two months after discharge still pale: apex beat outside the nipple line, presystolic apical murmur. X-ray: prominent right heart border, prominent pulmonary artery and conus.

CARDIOGRAPHIC FINDINGS (fig. 6).

RECORD A: Right axis deviation. S–T transition below the base line in lead II. P waves peaked in lead I and II.

In RECORD B, taken one month later, the P waves are notched in some cycles of lead I and II S–T segment below the base line in lead II and III. T wave sharply inverted in lead IV.

RECORD C: Taken two months after the onset of the carditis. The right axis deviation has become more marked, the T wave is flat in lead II. T inverted in lead III.

RECORD D: Three months after the onset of the carditis. The T waves have become smaller in lead I, flat in lead II, less inverted in lead III.

In RECORD E, taken four months after the onset of the carditis, the heart action is irregular due to premature beats. Right axis deviation. T wave sharply inverted in lead III.

RECORD F: Taken six months after the onset of the carditis. Right axis deviation. Premature beats of auricular origin. S–T segment depressed in lead I, T wave flat in lead I and II. T inverted in lead IV.

RECORD G: Taken 10 months after the onset of the carditis. Right ventricular preponderance. Premature beats of supra-ventricular origin in lead I, P–R. 0·19 second. Slurring of QRS in lead I and III, P diphasic in lead IV, QRS of Q type in lead IV.

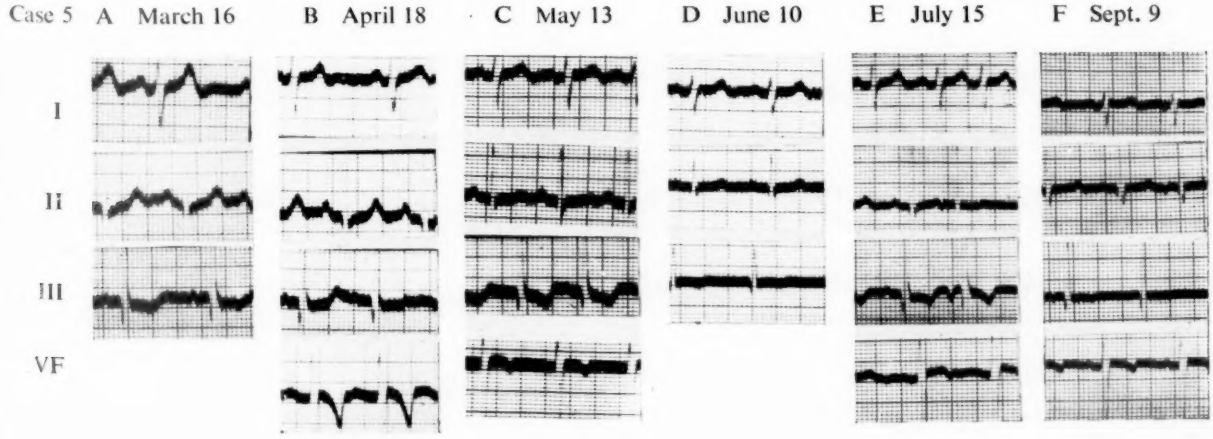

FIG. 6.

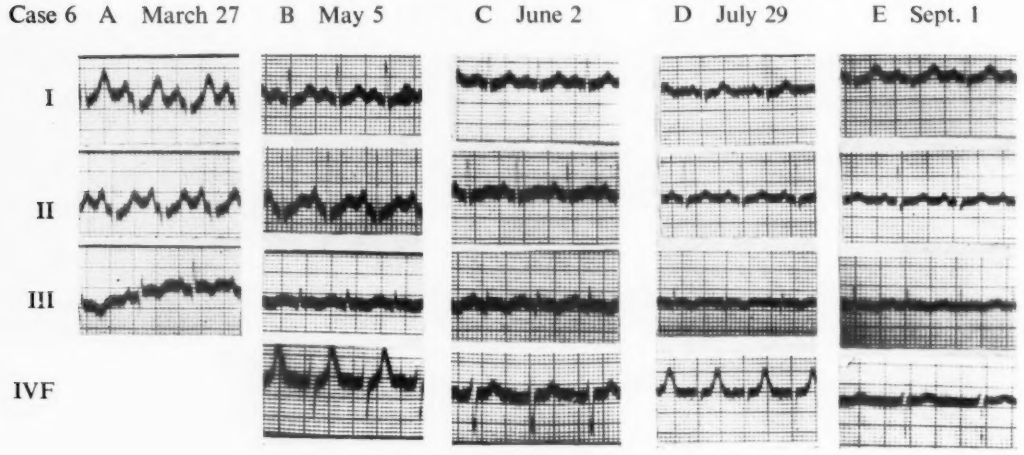

FIG. 7.

Case 6. J. K., 7 years. Stay in hospital 41 days. Previous diseases: measles, rubella, chicken-pox, mumps, pertussis, all of which occurred within the last two years. Onset of carditis on the 16th day of disease. Increased temperature for three days, persistent tachycardia, systolic apical murmur, high B.S.R. Two months after discharge pale, restless, poor sleep. Three months later: soon tired, lost 1½ lb. body weight in five weeks, poor appetite. Presystolic apical murmur. X-ray taken six months afterwards: right heart border and pulmonary conus prominent.

CARDIOGRAPHIC FINDINGS (fig. 7).

RECORD A: Sinus tachycardia, ventricular rate 143 per minute. P waves pointed in lead I and II. S–T segment below the base line in lead I and II. T wave inverted in lead III.

RECORD B: Sinus tachycardia, ventricular rate 159 per minute. S–T dislocated. T has become smaller and round in lead II. P peaked in lead II.

RECORD C: A follow-up record taken two months afterwards: the ventricular rate is about 150 per minute. Right axis deviation. T flat in lead II, the QRS has become inverted and the T wave much smaller in lead IV.

RECORD D: Taken four months after the onset of the carditis. Right axis deviation. S–T depressed in lead II, T wave flat in lead II.

RECORD E: Taken six months after the onset of the carditis. T wave flat in lead II and IV, inverted in lead III. QRS has a small upright phase and is mostly inverted in lead IV.

Case 7.

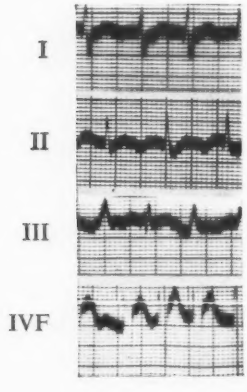

FIG. 8.

Case 7. L. A., 5 years. Previous diseases: measles, chicken pox within the last year. C. diphtheriae and S. haemolyticus present in throat swab. Onset of the carditis on the 11th day of disease. Syncope, gallop rhythm. Died on the 15th day of disease.

CARDIOGRAPHIC FINDINGS (fig. 8).

12th day of disease. Action irregular, no P waves are visible. Fine and coarse undulations, unequal in shape, timing and voltage between the ventricular deflections. Auricular fibrillation.

TABLE

THE CARDIOGRAPH FINDINGS IN 110 INVESTIGATIONS

Changes of the T wave			
flattening	40		
inversion	4	52 instances	47 per cent.
isoelectric	8		
S–T segment			
below the base line	44		
depressed	19	63 instances	57 per cent.
QRS			
of less than 1·5 mV voltage in all three limb-leads			18·16 per cent.
slurring		5 instances	4 per cent.
P wave			
peaked, of more than 0·3 mV voltage		25 instances	22·7 per cent.
right axis deviation		46 instances	42 per cent.
P–R prolonged			
auricular fibrillation		1 instance	
premature beats		6 instances	5 per cent.
tachycardia		15 instances	13 per cent.
Chest leads			
QRS			
inverted		22 instances	20 per cent.
of less than 0·8 mV voltage		6 instances	5 per cent.
slurring		3 instances	2 per cent.
T inverted *		13 instances	12 per cent.

* An inverted T wave might be found in the chest leads of healthy children or adolescents.

N.B. as regards the technique it is understood that all cardiograms have been taken with the patient in the recumbent posture.

Summary

1. Thirty-six cases of cardiac complications were observed amongst 602 cases of scarlet fever from August, 1943, till August, 1944.

2. Twenty-nine cases presented as myocarditis; two cases as partial auriculo-ventricular block; four cases as endocarditis; one case died of auricular fibrillation.

3. Clinical examination, blood sedimentation rate, cardiogram and x-ray findings were taken into consideration to ascertain whether heart disease was present or not. A follow-up examination of the patients after their discharge was found useful in arriving at the conclusion whether the cardiac damage was permanent or not.

Thanks are due to Dr. Ian McCracken, Medical Officer of Health, Newcastle upon Tyne, and Dr. G. Hurrell, Medical Superintendent, City Hospital for Infectious Diseases, for facilities provided.

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CASE REPORTS

PYELONEPHRITIS, MALIGNANT HYPERTENSION AND ULCERATION OF SMALL INTESTINE IN A CHILD

BY

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Cases of arteriolosclerosis in childhood have been reported frequently and an excellent review with a discussion of two cases was given by Guild, Kindell and Gibson (1938). Recently the relationship of pyelonephritis to arteriolosclerosis at all ages was emphasized by Weiss and Parker (1939), and this association in childhood has been reviewed by Kimmel (1942). Detailed records of single cases are now probably superfluous, but a case of chronic pyelonephritis developing malignant hypertension and arteriolonecrosis, and dying with extensive ulceration of the small intestine secondary to vascular lesions, presented certain interesting features. The relationship of these lesions is not yet widely appreciated by clinicians and pathologists and merits further study and discussion.

Clinical history. Six months before death the patient, a girl then aged twelve years, started to complain of severe headaches. One month later she was admitted to hospital. A trace of albumin and a few red blood cells were found in the urine and the blood urea was 80 mgm. per 100 c.c. One of two specimens of urine gave a growth of enterococci. A skiagram of the chest revealed nothing abnormal and the blood pressure was not recorded. She went home, but lost weight and became paler and was re-admitted three months before death. She still suffered from headaches of increasing severity and frequency. There was now slight oedema, the blood urea was 138 mgm. per 100 c.c. and the urine contained no pus or organisms, but continued until death to show a little albumin and some red blood cells. The blood Wassermann reaction was negative and a lumbar puncture revealed no abnormality. No record was made of the blood pressure. With rest the oedema disappeared and the blood urea fell, to fluctuate between 60 and 70 mgm. per 100 c.c. until death.

Though some complaint of abdominal pain was made four days before death there was no rigidity of the abdominal wall and no blood was noted in the stools. The patient gradually became more toxic and semi-comatose and died.

Post-mortem findings. The following is the anatomical summary of the findings after histological examination of all the organs. Only the more essential features will be described in further detail:

Bilateral chronic pyelonephritis with hyperplastic proliferative renal arterio- and arteriolo-sclerosis: chronic ureteritis and cystitis. Hypertrophy of left ventricle: arteriolosclerosis and early arteriolonecrosis in the adrenals, pancreas, spleen and stomach: arteriolosclerosis and marked arteriolonecrosis small intestine with multiple mucosal ulcers and localized fibrino-purulent peritonitis. Slight dwarfism (3 ft. 10 in.: normal 4 ft. 10 in.) without renal rickets or parathyroid dystrophy. Small areas of organized, unresolved pneumonia. Chronic venous congestion of lungs and slight splenic fibrosis. Chronic cholecystitis and cholelithiasis. Calcified primary tuberculous complex right lung.

KIDNEYS AND URINARY BLADDER. Both kidneys were small and the left weighed 15 gm. and the right 30 gm. The capsule was removed with difficulty, especially from the surface, over many deep scars. Everywhere its removal left a coarsely granular surface. The cortex was very narrow and often indistinguishable, and ill-defined and pale yellowish-white areas as well as several larger scars distorting the renal architecture. The pelves were not dilated and their lining epithelium was smooth. The ureters were thick walled and more patent than usual. There was no trabeculation or thickening of the bladder musculature and the lining epithelium showed no abnormality. The ureters opened normally and there was no obstruction in the urethra.

INTESTINAL TRACT. Loops of small intestine, especially the ileum, were loosely adherent to one another by a fibrinous exudate. This reaction was related to areas where the intestinal wall was eroded,

FIG. 1.—The mucosal ulcers in the anti-mesenteric border of the ileum.

but not completely perforated, by small, circular ulcers extending into the muscle from the mucosa (fig. 1). These ulcers lay in the anti-mesenteric segment of the bowel wall and few reached one centimetre in diameter. Seen from the mucosal aspect the ulcers and their surrounding zone of congestion and non-ulcerated areas of brown or gray diphtheritic membrane were sometimes confluent over ten to twenty centimetres of the anti-mesenteric border of the ileum. The mesenteric lymph glands and the lymphoid follicles of the bowel were not enlarged. The large intestine and the stomach showed congestion of the mucosa but no ulceration.

Microscopic examination.

KIDNEYS. In some areas the whole width of the kidney was atrophic and consisted only of tubules filled with colloid, lined by flattened epithelium and separated by fibrous tissue infiltrated by lymphocytes and a few plasma cells. Glomeruli were present only as hyalinized masses. In other areas (fig. 2) some renal tubules were larger and more dilated than normal, but many were atrophic and there were no entirely normal tubules. Here glomeruli were sometimes normal, but they often showed changes ranging from fibrosis around Bowman's capsule to complete hyalinization of the tuft and capsular tissues. They showed no epithelial proliferation and no adhesion of the tuft to the capsule. Even in these areas fibrous tissue was prominent, especially in the medulla between the larger collecting tubules. Inflammatory cells in the interstitial tissue were almost entirely mononuclear leucocytes. Similar cells were present in the sub-epithelial tissue of the renal pelvis and ureter and here fibrous tissue elements were replacing muscle fibres. Throughout the kidneys arcuate and interlobular arteries showed extreme proliferation of well formed and concentric elastic laminae (fig. 3). In the arterioles there was often considerable cellular proliferation and thickening of the wall, but there was little hyalinization and no fibrin or red blood cells disorganized the vessel walls (fig. 4).

ILEUM. Sections through the ulcers showed that these only rarely extended into the circular muscle coat. Necrotic fibrin, red blood cells and disintegrating polymorphonuclear leucocytes formed their floor. The submucosal tissue round an ulcer and usually all the muscle layers deep to it were oedematous and infiltrated by acute inflammatory cells and fibrino-purulent exudate lay on the adjacent serosa. Round the margin of the ulcers and forming the areas of diphtheritic membrane there were fibrin, red blood cells, polymorphonuclear leucocytes and the remains of the mucosal epithelium. The underlying submucosa was grossly congested and oedematous. Arterioles showed marked hyaline thickening of their wall and narrowing of their lumen, while fibrin and even red blood cells were often found in their wall. These arteriolonecrotic changes were not confined to the areas of reaction

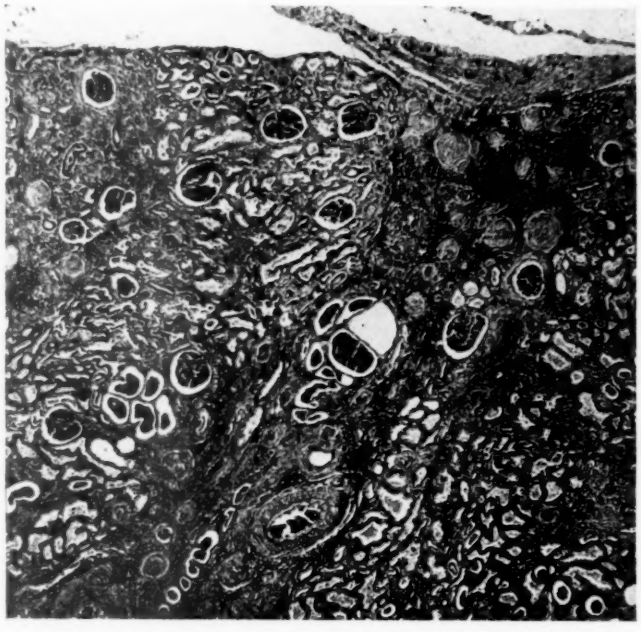

FIG. 2.—The capsule is adherent to a pyelonephritic scar and surviving renal elements are grossly distorted and fibrous tissue increased.

FIG. 3.—A collection of arteries showing proliferation of internal elastic laminae. Elastin stain.

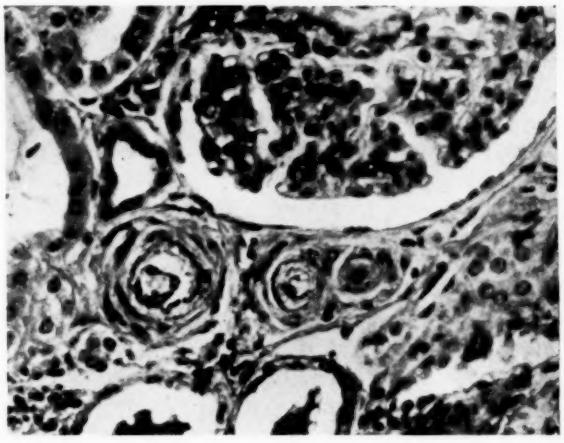

FIG. 4.—Arterioles narrowed by concentric cellular proliferation.

around the ulcers, but were also present, though to a lesser extent, in areas free from ulceration or mucosal inflammation.

THE INTIMATE VASCULATURE OF OTHER ORGANS. The walls of the arterioles of the pancreas, spleen, stomach, large intestine and adrenals were grossly thickened, sometimes by concentric cellular proliferation, but more often there was extensive hyalinization and sometimes fibrin was present in the wall. In the arteries there was no proliferation of the intima and no fibrosis of the media.

Discussion

In the past many cases of pyelonephritis have been misinterpreted both by clinician and pathologist. In chronic pyelonephritis the passage of organisms and pus cells may be slight and intermittent, and inadequate histological examination of small blocks of tissue taken at autopsy has often attributed the scarred and contracted kidneys to chronic glomerulonephritis or to benign or malignant hypertension. Even histological differentiation may be extremely difficult, but the coarse and more focal scarring of the kidney, the invasion of cortex, medulla, pelvis and even capsule by fibroblasts, lymphocytes, plasma cells and polymorphs are features favouring a pyelonephritis. It is doubtful if Weiss and Parker are correct in regarding colloid casts in the tubules as pathognomonic of pyelonephritis. In pyelonephritis, as in arteriosclerosis, all the glomeruli lying in large focal aggregates arranged at right angles to the capsule tend to be involved to much the same extent. The diffuse and varying involvement of glomeruli scattered throughout the kidney as seen in chronic nephritis is absent and adhesions of the tuft to the capsule are exceptional. Acute necrotic lesions in arterioles are not seen. In chronic pyelonephritis the arteries show gross proliferation of internal elastic laminae, and in the arterioles cellular hyperplasia without hyaline change narrows the lumen. Weiss and Parker maintain that these changes are the result of inflammatory changes in the tissues around the vessels and that they are to be distinguished from those secondary to parenchymatous atrophy. They believe that pyelonephritis often produces generalized hypertension, and they found in a large series of cases that the extent to which hyperplastic changes in the renal vessels were developed could be correlated with the development of clinical hypertension. They emphasize that in cases with hypertension the vascular changes are diffuse throughout the kidney and not confined, as in uncomplicated pyelonephritis, to areas of gross post-inflammatory scarring, and that vascular lesions in the kidney are in excess of those elsewhere in the body.

In the present case there is unequivocal histological evidence of chronic pyelonephritis. Though no blood pressure readings are available the hypertrophy of the left ventricle in the absence of valvular lesions, and the widespread arteriolosclerosis are satisfactory evidence of hypertension. The escape of fibrin and red blood cells into the walls of arterioles, especially those of the intestinal tract, suggests that there was a malignant termination to this hypertension. The proliferative lesions narrowing the lumen of the renal arteries and arterioles are diffuse throughout the kidneys and in excess of those elsewhere in the body. Weiss and Parker would regard the renal vascular changes as secondary to pyelonephritis, probably exaggerated somewhat by the resultant hypertension. It may be possible, as they claim, to predict the occurrence of hypertension from the extent of the narrowing of the renal vessels alone. It is an attractive speculation to consider that the reduction of the lumen of these vessels by the proliferative reaction, secondary to the inflammation of pyelonephritis, proceeds in advance of the loss of renal parenchymatous tissue. The resultant ischaemia of renal tissue might then lead to a hypertension comparable to that following narrowing of the renal artery by a clamp as in the classical experiments of Goldblatt. In growing children the fibrosed kidney with its damaged vascular system cannot develop with the growth of the child. This is paralleled by the experiments of Drury (1938). He encircled, but did not constrict, the left renal artery of young rabbits with a ligature. With the growth of the animals hypertension developed, and this was exaggerated by the renal insufficiency which followed removal of the right kidney. The development of hypertension in a patient will depend on the amount of functioning renal tissue surviving as well as on the establishment and maintenance of a delicate balance between ischaemia and death in the kidney tissue supplied by the narrowed vessels. Pyelonephritis may be accepted as responsible for a high percentage of the few cases of hypertension in childhood and must always be excluded in such cases. In adults it is more difficult to decide how far a co-existing pyelonephritis is responsible for the initiation of hypertension and not merely an incidental association.

In this case a feature of considerable interest is the ulceration of the small intestine in the absence of uraemia.

Fishberg (1939) describes ulceration and necrosis as a complication of uraemia and does not consider it apart from uraemia as a complication of hypertension. Several case reports of hypertension without uraemia in childhood describe, but do not discuss, intestinal lesions similar to those of the present case (case 11 of Weiss and Parker and case 1 of Guild et al.). Jaffe and Laing (1934) found ulceration in 27 of 136 cases with blood urea varying from 50 to 250 mgm. per 100 c.c. They quote Siegmund, who was inclined to associate uraemic intestinal necrosis and ulceration with lesions of the arterioles. They found, however, that vascular necroses were always in close proximity to the necrosis of the mucosa and regarded them as secondary and as comparable to the arteriolar necroses of dysenteric ulceration. They regard the uraemic necrosis and ulceration as secondary to haemorrhages from small blood vessels the permeability of which is altered by some substance in the blood associated with the uraemia. In the

present case submucosal haemorrhages very probably preceded the ulceration, but they were secondary to arteriolar lesions like those studied by Goldblatt (1938) in the intestine of dogs with experimental malignant hypertension.

The case provides no direct evidence as to whether a toxic factor retained by damaged kidneys is necessary for the development of arteriolonecrosis as well as a high intra-lumen bursting tension. It is interesting to note that the arterioles in the kidney itself have been protected from necrosis by the proliferative changes narrowing the arteries, and this may be compared to the similar protection of the renal arterioles by the clamp narrowing the renal artery in Goldblatt's hypertensive dogs.

The patient was 12 inches under the normal height for her age. Ellis and Evans (1933) describe rickets, dwarfism and infantilism as secondary to renal insufficiency in childhood. All of these were not necessarily present in any one case. Histologically there was no irregularity of the epiphyseal junctions in the present case and she was too young to show genital infantilism. Most of the cases of Ellis and Evans were due to bilateral hydronephrosis with or without infection. Usually no organic lesion was demonstrable in the urethra, the bladder was dilated and a sphincteric imbalance was postulated. In the present case the cause of the pyelonephritis is obscure and there was no bladder outlet obstruction.

Between her first and second admission there was some cardiac decompensation as shown by the slight oedema and the high blood urea of 138 mgm. per 100 c.c. This improved with rest, but slight chronic venous congestion of the lungs and fibrosis of the spleen persisted. The small areas of unresolved pneumonia probably date from about the time this decompensation was most apparent, and some such infection may have contributed to its development.

Summary

Malignant hypertension in a child of twelve years followed chronic pyelonephritis. Ulcers in the ileum secondary to hypertensive lesions in the arterioles produced a terminal peritonitis.

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CONGENITAL THROMBOCYTOPENIC PURPURA

BY

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Congenital thrombocytopenic purpura is a rare condition. A review of the literature fails to show any case reported from this country. In 1925 Rushmore was able to find seven examples of purpura in pregnancy in which both mother and child were affected, but the type of purpura was not specified. Since that time congenital thrombocytopenic purpura has been recorded on fourteen occasions with eight thrombocytopenic mothers (see table 1). The following instance in a newborn infant whose mother did not suffer from the disease may therefore be of interest.

Clinical details

A male infant, three days old, was admitted to the Hospital for Sick Children, Great Ormond Street, on April 21, 1944, with a purpuric eruption. He was born at term following an uneventful pregnancy and labour. On the second day of life purpuric spots were first noticed on the buttocks and extended rapidly to the legs and scalp. Jaundice also appeared at this time. His parents and one older sister were healthy, but the second sister suffered from recurrent epistaxis.

Examination showed a normally responsive, well-nourished baby, weighing 5 lb. 14 oz. T. 100·2° F. (rectal), P. 140, R. 40. A diffuse purpuric rash was present over all areas of the skin and also on the hard palate with small ecchymoses on the back and legs; mild jaundice was present; mucous membranes were a good colour; the spleen was not palpable; and there was no abnormality of heart, lungs, abdomen or central nervous system. No evidence of infection was found. The urine and stools were free from blood. Pathological investigations carried out on the fourth day were as follows:—

INFANT:

Blood count:	R.B.C.	6,700,000 per c.mm.; Hb. 130 per cent. (Sahli); C.I. 0·97.
	W.B.C.	13,300 per c.mm.
	Polymorph.	58 per cent. with 38 per cent. stab forms.
	Lymphocytes	37 per cent.
	Monocytes	1 per cent.
	Eosinophils	4 per cent.
	No immature cells seen.	
Platelet count		6000 per c.mm.
Bleeding time		10 minutes (Duke's method—normal 2–5 minutes).
Prothrombin time		26 seconds (McTookey's method—normal 11–15 seconds).
Blood group O		Rh-positive.

MOTHER:

Platelet count	350,000 per c.mm.
Blood Wassermann reaction	negative.
Blood group O	Rh-positive.

No abnormal antibodies were present in the serum.

The infant remained in hospital for four weeks, during which time he made good progress, gaining 20 oz. in weight. The purpura faded gradually; a few new lesions appeared during the first fortnight; the stools contained streaks of bright blood from time to time and there was one small haematemesis. He was symptom free by the end of the third week. Apart from a temperature of 100° F. on admission he was afebrile, his rectal temperature varying between 97·6° F. and 99° F. for the first eight days and then becoming stabilized at 98° F. No infection was detected at any time. The jaundice continued for eighteen days which is considerably longer than usual in physiological jaundice; the fall in the red blood count was also marked (see table 2). In spite of clinical improvement the thrombocytopenia persisted with a platelet count of only 10,000 per c.mm. on discharge from hospital at one month old (see table 2). The normal figures for the neonatal period are 200,000–300,000 per c.mm. (Sanford, 1942).

The patient was not seen again until he was six months old because of the danger from flying-bombs in the London area. During the interval he had remained symptom free although he had had a severe attack of bronchitis. The platelets had risen to 350,000 per c.mm. and the bleeding time had fallen to 5½ minutes.

This was a spontaneous recovery. The only treatment the child received was vitamin K (5 mgm. kapilon intramuscularly) on admission and liver (Armour's Proethron forte 2 c.cm.) given on the twenty-first and twenty-third days, the latter being without effect on the thrombocytes. Owing to the benign clinical course blood transfusion was not considered necessary.

Comment

This appears to be an undoubted example of congenital thrombocytopenic purpura. The rash was noticed by the second day and the platelets were reduced to 6,000 per c.mm. on the fourth day. A symptomatic purpura was unlikely as no infection was found, no drug liable to cause a thrombocytopenia had been given to mother or child, and in spite of the prolonged jaundice no other blood disease was demonstrable.

In nine of the cases reviewed the condition was

TABLE 1.—CASES OF CONGENITAL THROMBOCYTOPENIC PURPURA

Reference	Manifestations	Platelet count per c.mm.	Bleeding time (minutes)	Treatment	Course	Family
WALTNER (1924)	Purpura of skin at birth.	90,000	12	None.	Marked icterus; some sepsis. Symptom free by seven months.	Mother: purpura at seventh month of pregnancy. Platelets 50,000. Bleeding time 27 minutes.
LESCHKE (1926)	Purpura of skin at birth with haematuria and melaena.	0	12–15	None.	No bleeding after tenth day.	Mother: purpura at fifth month of pregnancy. Platelets 60,000.
LIEBLING (1926)	Purpura of skin at birth with haematemesis and melaena.	40,000	—	Haemoplastin, 5 c.cm. intramuscularly.	Did well. Purpura faded at one month. Platelets 240,000.	Mother: purpura at fifth month of pregnancy. Platelets 40,000.
GREENWALD (1929)	Purpura of skin appeared on fifth day.	30,000	5	None.	Died on seventh day. Congenital morbus cordis. Thrombocytes scanty and abnormal in appearance.	—
BAYER (1931)	Purpura of skin at birth.	50,000	40	None.	No fresh bleeding after birth. Platelets 320,000 by second year.	—
Ibid.	Purpura of skin at birth.	48,000	6½	None.	No fresh bleeding after birth. Platelets 150,000 on fifth day.	Twin. Platelets 77,000. Bleeding time 1 minute. No symptoms.
Ibid.	Purpura of skin and mucous membranes at birth : with haematemesis and melaena.	45,000	11	Coagulen and gelatin intramuscularly.	No fresh bleeding after fifth day. Platelets 280,000 by second year.	—
Ibid.	Purpura of skin at birth. Haematemesis on second day.	50,000	90	None.	Died on second day. Widespread purpuric lesions.	—
GUTTFREUND (1933)	Purpura of skin and mucous membranes at birth.	0	40	90 c.cm. blood intramuscularly, also blood transfusion (? amount).	Continued to bleed. Died of pneumonia at four months.	Father: severe epistaxis and excessive bruising. Mother: Platelets 32,000, but symptom free.
SANFORD (1936)	Purpura of skin at birth.	20,000	—	None.	No fresh lesions after birth. Platelets 137,000 by tenth day. Mother and child both showed increased disintegrating power of platelets.	Mother: recurrent purpura. Platelets 17,500.
DAVIDSON (1937)	Purpura of skin at birth.	56,000	3	Blood, 100 c.cm. intramuscularly without improvement. Bothrops antitoxin, 5 c.cm. intramuscularly with clinical recovery.	Platelets 672,000 by ten weeks. Remained normal for two years.	Mother : splenectomy eight years before for thrombocytopenic purpura. Platelets 6,000–50,000.
WHITNEY (1942)	Purpura of skin at birth.	80,000	1	Blood intramuscularly, 20 c.cm.	Died third day. Tentorial tear. Widespread purpura.	Mother of these two infants had splenectomy at fourteen years of age. Platelets 70,000.
Ibid.	Purpura of skin at birth.	90,000	11	Blood intramuscularly, 55 c.cm., twice.	Died second day with multiple haemorrhages.	
URBANSKY (1942)	Purpura of skin and mucous membranes.	23,200	5¼	50 c.cm. blood intravenously.	Purpura faded in a few days. Bleeding time 1½ minutes at 2½ years old.	Mother had splenectomy six years previously for thrombocytopenic purpura. Platelets 75,000 at six months of pregnancy.

TABLE 2

Date	Hb. per cent.	R.B.C. per c.mm.	W.B.C. per c.mm.	Platelets per c.mm.	Bleeding time
22.4.1944	130	6,700,000	13,300	6,000	10 minutes +
1.5.1944	80	3,500,000	22,200	7,000	—
8.5.1944	80	4,100,000	16,000	15,000	10 minutes +
12.5.1944	—	—	—	12,000	—
26.5.1944	—	—	—	10,000	—
24.10.1944	—	—	—	350,000	5½ minutes

familial; in the four collected by Bayer the mothers' platelet counts were not noted. In the present instance the mother's blood was normal and she had never shown a tendency to bleed.

The prognosis in these infants is of some interest. Nine of the fourteen recovered during the first few weeks of life but their progress was not followed further except in three who remained healthy for two years. It would be instructive to know whether or not these children tend to relapse later in life. Five of the infants died, associated lesions may have been the cause of death in three of them. Two only died of uncomplicated purpura. Thus prognosis does not appear to be so grave as might be expected.

From a study of these reports therapy seems to have had little effect. Five infants recovered without treatment. Blood transfusions in adequate amounts would seem to be the rational treatment in any severe case. The advisability of splenectomy at birth was discussed by Whitney (1942) but in view of the above figures does not appear justifiable.

Summary

A case of congenital thrombocytopenic purpura is reported.

Examples of congenital thrombocytopenic purpura collected from the literature are tabulated.

The prognosis and treatment of the condition is considered.

Thanks are due to Dr. W. G. Wyllie for permission to publish this case.

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